Supplementary Data C – Case notes for primary outcomes (individual patient numbers removed)

Supplementary data Table 1 All cause mortality (deaths) prior to randomisation: 2 deaths, one on placebo and one on SSRI (duloxetine)

Trial	Start date FPFV	End date LPLV	Condition	Duration of LI period	Drug	Case notes on the death
HMBC	March 2002	July 2003	MDD	12 weeks 533 patients entered an open label single arm LI phase with DLX at v2 for 12 weeks prior randomisation**	DLX open label 60mg/ day	**38Y M patient, at v5 on day 16** Completed suicide by hanging *"..The patient had an 8 year history of suffering from depression without suicidal ideation .....The patient reported the adverse events of night sweats and hot flashes that were still ongoing at the time of death. ...His HAMD item 3 suicide risk score was 1-feeling life is not worth living throughout the trial."*
050-334	Feb. 1992	Feb. 1993	MDD or bipolar depression	4-14 days Single blind PLB LI prior to the 6 weeks of acute phase*	PLB LI	**No patient details available** Death by natural causes "*The investigator was informed by his relatives that death had been ascribed to natural causes and no autopsy had been performed."* No further details available.

FPFV: first patient, first visit; LPLV: last patient last visit; LI: lead-in phase of trial
DLX: duloxetine; PLB: placebo;
Feb.: February; HAMD: Hamilton Rating Scale for Depression; M: male; MDD: major depressive disorder; v: visit number; Y: years
* The study had varying LI phase lengths. 3 patients in SER had no LI phase and went to active treatment at screening. 4 patients in PLB arm had concomitant therapy with antidepressants (TCA or other similar) but whether this patient was on any other medication was not noted.
** There were 533 patients on DLX for 12 weeks open label and this was followed by a total of 278 patients who continued the study and were randomised at v8 to either receive PLB (142) or DLX (136) for a further 26 weeks.

Supplementary data Table 2 All cause mortality (deaths) in acute or randomisation phase: 12 deaths, three on placebo, eight on SSRI and one on imipramine

Trial	Start date FPFV	End date LPLV	Condition	Duration of study phase	Drug	Case notes on the death
HMATa	March 2000	April 2001	MDD	8 weeks This trial had a 1 week PLB LI and a 2 week PLB LO phase after the 8 weeks acute phase.	DLX 40mg/day	**78Y M patient, at v9 on day 60** Cardiac-respiratory arrest resulting in death *"…. Patient's niece notified the site that the patient threw all his study medications away on 8-Sep-00 and no longer wanted to participate in study. The patient refused to return to the site for an early discontinuation visit, and thus was terminated from the study on 11-Sep-00. On 12-Sep-00, the patient's niece went to the patient's home and found him lying on his back and apparently dead.... An autopsy was not performed at the family's request. The death certificate indicated the immediate cause of death as cardio-respiratory arrest.."*
HMAYa	Nov. 2000	July 2002	MDD	26 weeks EXT/ CONT This was the continuation phase (Study Period III) for responders.*	DLX 40mg/day	**44Y F patient, at v14 on day 216** Non-cardiogenic pulmonary oedema resulting in death "*..The patient had a history of hospitalization for worsening of psychotic symptoms in June 2000... On 9 December 2001 the patient had an argument with her husband which made her quite upset, even the following day. During the 9th and 10th of December the patient complained of chest pain (pressure) which a family friend considered a psychiatric symptom. On 11Decemberthe friend attempted to contact the patient but she never answered the phone. The friend then went to the patient's house only to find her lying in bed, barely conscious, no fever, no vomiting. The patient was incontinent of urine in bed ….admitted to taking 5 tablets of oxazepam..."*
HMAYa	Nov. 2000	July 2002	MDD	26 weeks EXT/ CONT This was the continuation phase (Study Period III) for responders.*	DLX 60mg/day	**23Y F patient, at v9 on day 82** Completed suicide by jumping out of a window. **"...."***The patient had been taking cetirizine hydrochloride and budesonide since 1996 for asthma. ...on 15-Jan-02, before having breakfast, the patient went to the bathroom and asked her grandma to wait breakfast for her. When breakfast was ready she suddenly went to her room and jumped out the window. The patient gave no warning or explanation for her actions. The patient died. She had been treated*

Trial	Start date FPFV	End date LPLV	Condition	Duration of study phase	Drug	Case notes on the death
						for the past 4 years by the investigator with no previous suicide attempts. The patient was a good student but did have some relationship problems with her mother....."
HMAYa	Nov. 2000	July 2002	MDD	26 weeks EXT/ CONT This was the continuation phase (Study Period III) for responders.*	PLB	**53Y F patient, at v14 on day 222** Completed suicide by hanging. *"..On 30-May-200l the patient began placebo ...on 16 November2001 the patient reported stomach pain so the investigator prescribed omeprazole.....on 21 December 2001 Betacid was prescribed for hypoacidity. On 27 December the patient reported insomnia and began taking zopiclone. The patient again reported insomnia on 3 January 2002 and 5 January 2002 so the investigator suggested that the patient be discontinued from the study. The early termination visit was scheduled for 7 January, but the patient did not attend that visit and on 8 January the patient's husband called to inform the site that the patient hung herself (completed suicide) on 7 January 2002.... The patient had no previous suicide attempt."*
HMAW	June 2001	April 2003	DPNP	12 weeks No LI phase. Patients who completed were reallocated to an extension study**	PLB	**73Y M patient , on day 3** Accidental drowning resulting in death *"..The patient had a history of hypertension and hypertriglyceridemia since 1992, and a stroke that had occurred in June 2001. The patient also had a history of diabetes mellitus since 1995. The patient began placebo on 19 December 2001....On 22 December 2001, 3 days after starting placebo, the patient's wife found him dead in the hot tub. ...No autopsy was performed."*
HMAW	June 2001	April 2003	DPNP	52 weeks EXT/ CONT This was the continuation phase (Study Period III) **	DLX 60mg/ day	**No patient details available** 1 patient had SAE of sepsis and died No further details available.
HMAW	June 2001	April 2003	DPNP	52 weeks EXT/ CONT This was the continuation phase (Study Period III) **	DLX 60mg/ day	**No patient details available** 1 patient had SAE of myocardial infarction and died No further details available.

Trial	Start date FPFV	End date LPLV	Condition	Duration of study phase	Drug	Case notes on the death
SBAX	May 2001	May 2002	SUI for Women	12 weeks The trial had a 2 week PLB LI period and those that completed the study could enter trial SBBM	DLX 80mg/ day	**70Y F patient at v14 on day 222** Multifocal embolic cerebrovascular accident resulting in coma and her eventual death "*...Approximately 5 weeks after receiving study drug, the patient had complaints of painful chest muscles after lifting heavy rocks in her garden. The patient consulted with her physician and was prescribed Diclogenac and Synap Forte. An x-ray was performed and showed two fractured ribs. On 15-Sep-2001, this patient was found in semi-comatose state... experienced a multifocal embolic cerebrovascular accident resulting in coma.... the patient was intubated and a chest x-ray confirmed the presence of rib fractures and showed a left haemothorax. The investigator suggested that the patient may have fallen, which caused the previously fractured ribs to puncture her lung and cause the haemothorax. This required surgical drainage. The haemothorax was thought to complicate her already depressed respiratory function. Benzodiazepine level was higher than normal range, but the patient reported no benzodiazepine concomitant medications.*
0600B-367-EU	Oct. 1994	Sept. 1995	MDD	8 weeks Study had 7 ± 10 days LI and to up to 3 days of taper LO phase followed by 4-10 days of PT.	VEN ER 75 mg/day	**62Y F patient on day 26 (suicide attempt on day 21)** Completed suicide by strangulation (was hospitalised, but ultimately died), noted as post-study event in CSR *"... She was randomly assigned to receive venlafaxine ER 75 mg/day on November 8, 1994. ...Her husband described her as having ´a good day´ on November 27 with nothing to predict her suicidal behavior on the following day. On November 28, she attempted suicide by strangulation (hanging). She was hospitalized and resuscitated before being transferred to an intensive care unit. ..... During the night of December 2 further neurologic deterioration appeared; an angiography showed there was no intracerebral blood flow which was compatible with cerebral death. She died on December 4."*
0600B 1-384-US/ EU/CA	Sept. 1997	Nov. 1999	MDD	6 weeks The trial had a 7 ± 4 days of PLB LI planned but was not followed strictly. The	IMI 125mg/ day	**54Y M patient, on day 25** Completed suicide by hanging. *"On 14 Feb 99, the patient committed suicide by hanging. The patient was brought to the hospital, but died despite attempted resuscitation. He was not reported as having been suicidal before and had shown significant clinical improvement during the study."*

Trial	Start date FPFV	End date LPLV	Condition	Duration of study phase	Drug	Case notes on the death
				LO varied as well***		
050-113	Oct. 1988	Jan. 1992	NID DM	54 weeks Summary report with limited data and no protocol as clinical programme was terminated due to lack of efficacy. The trial noted no LI nor LO study phases****	PLB	**58Y F patient on day 404** Myocardial infarction leading to death. Listed in randomised phase in CSR *"This 58-year-old female, with diabetes mellitus and a history of angina pectoris, received double-blind placebo in this study. Study drug was administered orally from March 30, 1989, to May 6, 1990, a total of 403 days. On May 7, 1990 she suffered an acute myocardial infarction and died."*
648	Feb. 1999	Feb. 2000	PTSD	12 weeks Study had 1 week LI and 2-3 weeks double blind tapering with a 2 week follow up PT	PAR	**38Y M patient, on day 63 and 21 days after last dose** Accidental overdose with ethyl alcohol and PAR noted as post-study event in CSR *"...patient entered R phase on 22-June-1999 & was later terminated from the study due to drinking, protocol violations. Last dose of study medication was reportedly taken on 03-August-1999 and patient's grandmother noted that on 23-Aug-1999, the patient seemed "confused and was hallucinating." On 24-August-1999, approximately 63 days after receiving the first treatment with blinded study medication, and 21 days after receiving the last treatment with blinded study medication, the patient was found dead in his truck with no evidence of external injury or trauma. Toxicology results revealed a high concentration of ethyl alcohol 0.37%. Paroxetine was also detected at 0.58mcg/ml.*

DLX: duloxetine; PLB: placebo; VEN ER: venlafaxine extended release
FPFV: first patient, first visit; LPLV: last patient last visit; LI: lead-in phase of trial; LO: lead-out phase of the trial; EXT/ CONT: extension phase of the trial
DPNP: diabetic peripheral neuropathic pain; F: female; HAMD: Hamilton Rating Scale for Depression; M: male; MDD: major depressive disorder; NIDM: patients with non-insulin-dependent diabetes mellitus, treatment for obesity; Nov.: November; Oct: October; SAE: serious adverse event; Sept.: September; SUI: stress urinary incontinence; v: visit number; Y: years
* The report stated that the "established criteria for entry into Study Period III will be blinded to investigator site staff and subjects." The report states that the criteria were described in the IRB Supplement 1 as part of the appendices. This appendix was however unavailable to us.

**Patients who completed the acute phase of the trial were then randomly reallocated to treatment with DLX 60 mg/day or routine care to further the study for an additional year. We did not have access to the results of this phase; data was only available from the Lilly online summary reports.

* **The results state that PLB LI was for 3-11 days but 1 patient is listed as having only 1 day of LI. The LO planned was tapering of dose for 3 weeks, but only 1 week for Europe, however taper phase could be omitted or adjusted (up to 21 days in US and CA; 10 days in EU) if medically indicated. Data from 4-10 days after therapy was also noted. The death of this patient occurred on day 21 but as the patient was hospitalised.

** **The summary report states "Rationale for Providing a Summary Report: Due to the lack of meaningful long-term effectiveness of sertraline in reducing body weight there will be no further development of this clinical program..... A detailed analysis of the safety of sertraline on all 356 subjects who were enrolled in this clinical trial was reported on 5 April 1994." We did not have access to this detailed analysis. The death occurred on day 404 which is after the 54 week study mark but the narrative suggests that the patient was taking PLB till 1 day prior.

Supplementary data Table 3 All cause mortality (deaths) in lead-out (LO) and/ or post-therapy phases (PT): 2 deaths, one on placebo and one on SSRI (venlaflaxine extended release)

Trial	Start date FPFV	End date LPLV	Condition	Duration of study phase	Drug	Case notes on the death
0600B 1-384-US/EU/CA	Sept. 1997	Nov. 1999	MDD	10-21 days of LO phase.* The trial had a 7 ± 4 days of PLB LI and an acute phase of 6 weeks.	VENER 375 mg/ day	**28Y M patient, 3 months after last dose** Cause of death unknown *"...On 20 March 1999, the patient suffered a minor injury. On 8 April 1999, he was hospitalized because of an infection at the injury site. Intravenous antibiotics were given and he subsequently recovered after treatment. Study drug had been discontinued because the patient did not take the medication to the hospital. On 21 July 99, 3 months post study, the patient was found dead. After autopsy, the cause death remained unknown."*
627	July 1998	Jan. 2000	PTSD	Up to 3 weeks of double blind tapering LO phase, followed by 14 days PT (but could range from 2 to 6 weeks PT) ** The trial had a 1 week PLB LI and an acute phase of 12	PLB	**39Y M patient, 17 days after last dose** Completed suicide by shooting *"....The patient received oral study medication (placebo dose level 1) from 13 February 1999. On 19 February 1999, some 7 days after the first dose the patient experienced severe depressive symptoms, which worsened over the next 2-3 weeks. During this time, the patient experienced extreme post-traumatic stress disorder symptoms, including strong feelings of agitation, social withdrawal and* ***suicidal ideation****. ....The patient was diagnosed as having acute depression. The patient was treated for the event with*

Trial	Start date FPFV	End date LPLV	Condition	Duration of study phase	Drug	Case notes on the death
				weeks.		***clotiapine, oxazepam*** *and* ***fluoxetine.*** *Treatment with study medication was stopped due to the depression on 01 March 1999 and the patient was withdrawn from the study. ... On 15 March 1999, the patient underwent electroconvulsive therapy as an out-patient (last treatment of 6) and his condition was reported as much improved. ...On 18 March 1999, some 17 days after the last dose of study medication, the patient committed suicide by shooting himself. "*

PLB: placebo; VEN ER: venlafaxine extended release
FPFV: first patient, first visit; LPLV: last patient last visit; LI: lead-in phase of trial; LO: lead-out phase of the trial;
Jan: January; M: male; MDD: major depressive disorder; Nov.: November; PT: post therapy; PTSD: posttraumatic stress disorder; Sept.: September; v: visit number; Y: years

Supplementary data Table 4 Total number of competed suicides: 6 completed suicides, 1 prior to randomisation, 4 in the acute phase and 1 post therapy (case notes above in mortality tables)

Trial	Start date FPFV	End date LPLV	Condition	LI period	Drug and daily dose	Completed suicides prior to randomisation
HMBC	March 2002	July 2003	MDD	12 weeks	DLX 60mg open label LI	38Y M patient, at v5 on day 16 Completed suicide by hanging

Trial	Start date FPFV	End date LPLV	Condition	R period	Drug and daily dose	Completed suicides in the acute or randomised phase
HMAYa	Nov. 2000	July 2002	MDD	26 weeks EXT/ CONT	DLX 60mg	23Y F patient, at v9 on day 82 Completed suicide by jumping out of a window.
HMAYa	Nov. 2000	July 2002	MDD	26 weeks EXT/ CONT	PLB	53Y F patient, at v14 on day 222 Completed suicide by hanging.
0600B-367-EU	Oct. 1994	Sept. 1995	MDD	8 weeks	VEN ER 75 mg	62Y F patient on day 26 (suicide attempt on day 21) Completed suicide by strangulation (was hospitalised, but ultimately died).
0600B 1-384-US/ EU/CA	Sept. 1997	Nov. 1999	MDD	6 weeks	IMI 125mg	54Y M patient, on day 25 Completed suicide by hanging.

Trial	Start date FPFV	End date LPLV	Condition	Duration of LO/PT phase	Drug and daily dose	Completed suicides in the post therapy phase
627	July 1998	Jan. 2000	PTSD	14 days PT (but could range from 2 to 6 weeks PT)	PLB	39Y M patient, 17 days after last dose Completed suicide by shooting

FPFV: first patient, first visit; LPLV: last patient last visit; LI: lead-in phase of trial; R: randomised or acute phase of trial; LO: lead-out phase of the trial; EXT/ CONT: extension phase of the trial
DLX: duloxetine; IMI: imipramine; PLB: placebo; VEN ER: venlafaxine extended release
Jan: January; F: female; M: male; MDD: major depressive disorder; Nov.: November; Oct.: October; PT: post therapy; PTSD: posttraumatic stress disorder; Sept.: September; v: visit number; Y: years

Supplementary data Table 5 Number of suicide attempts (SA), (including intentional overdoses and intentional self-harm) pre-randomisation: 6 events, 4 on SSRI (duloxetine) and 2 on placebo

Trial	Start date FPFV	End date LPLV	Condition	Duration of LI/ screening	Drug and daily dose	Case notes on the suicide attempts
HMBC	March 2002	July 2003	MDD	12 weeks 533 patients entered an open label single arm LI phase with DLX at v2 for 12 weeks prior randomisation*	DLX 60mg open label LI	**39Y F patient, at v4 on day 11** Intentional overdose on Stilnox *The patient reported two previous episodes of major depression but no history of any previous drug therapy for depression... On 22 September 2002, 11 days after starting study drug, the patient attempted suicide by over dosing on Stilnox 50mg....The patient had no previous history of suicide attempts prior to this event. The patient was discontinued from the study and hospitalized due to patient verbalizing another possible attempt."* The patient had concomitant therapy with zolpidem.
HMBC	March 2002	July 2003	MDD	12 weeks 533 patients entered an open label single arm LI phase with DLX at v2 for 12 weeks prior randomisation*	DLX 60mg open label LI	**30Y F patient, at v7 on day 54** Intentional overdose on DLX, diclofenac sodium and tetrazepam *"The patient started open label duloxetine on 8 October 2002 for Major Depressive Disorder. On 30 November 2002, after an argument with her husband, the patient made a suicide attempt by ingesting all her remaining study medication (about 54 capsules) and 2 capsules of diclofenac sodium (Voltaren) and 2 capsules of tetrazepam (Myolastin).....The patient was hospitalized and treated with gastric lavage and active charcoal. A drug screen was positive for benzodiazapines..... The patient did not experience any events resulting from the overdose... The patient's last dose of study drug was 30 November 2002...discontinued from the study on 3 December 2002."*
HMBC	March 2002	July 2003	MDD	12 weeks 533 patients entered an open label single arm LI phase with DLX at v2 for 12 weeks prior randomisation*	DLX 60mg open label LI	**25Y F patient, at v5 on day 20** Intentional overdose on DLX *"The patient had no previous history of suicide attempt and had one previous episode of major depression ....On 2 October 2002 (visit 4), 9 days prior to event, the patient's HAMD score had dropped to 16 and suicide item# 3 to a score of 0. On 13 October 2002, the patient attempted suicide by ingesting 24 capsules of*

						study drug....The patient immediately reported it to her mother who then took her to the emergency room....The patient had no history of previous suicide attempt noted."
HMBC	March 2002	July 2003	MDD	12 weeks 533 patients entered an open label single arm LI phase with DLX at v2 for 12 weeks prior randomisation*	DLX 60mg open label LI	**No patient details available, at v5** Possible suicide attempt This event was only listed in the appendix within the tables for all adverse events for all patients. The event was "possible suicide attempt" at visit 5, mild for a different patient to the ones listed above during the open single blind DLX phase. No further details are available from the CSR.
377	April 1995	May 1998	MDD paediatric	2 weeks LI. Acute phase was 12 weeks with a 2 weeks LO taper phase of PAR	PLB LI	**17Y F patient, during PLB LI, day unknown** Intentional overdose on bromazepam and valium "*During the screening period the patient experienced moderate emotional lability and tried to overdose on bromazepam.....No other corrective therapy was given....On 24 January 1997, during the placebo run-in and prior to study medication, the patient took an intentional overdose of bromazepam and valium. .... She experienced no side effects as a result of the overdose....the patient had problems at home and had recently had a fight with her boyfriend.*"
377	April 1995	May 1998	MDD paediatric	2 weeks LI. Acute phase was 12 weeks with a 2 weeks LO taper phase of PAR	PLB LI	**15Y F patient, on day 29 (unclear why still on PLB run in)** Slitting of wrist "*On 12 November 1996, the patient started taking 29060 (placebo run-in) for depression. Approximately twenty four days later on 5 December 1996, the patient impulsively slit her wrists following an altercation with her mother. The wounds were superficial and were not stitched. The patient was withdrawn from the study on 10 December 1996, before any active medication was received, because of the poor response by the patient, the parasuicide and the risk of further attempts."*

DLX: duloxetine; PLB: placebo
FPFV: first patient, first visit; LPLV: last patient last visit; LI: lead-in phase of trial; LO: lead-out phase of the trial;
F: female; M: male; MDD: major depressive disorder; v: visit number; Y: years
* There were 533 patients on DLX for 12 weeks open label and this was followed by a total of 278 patients who continued the study and were randomised at v8 to either receive PLB (142) or DLX (136) for a further 26 weeks.

Supplementary data Table 6 Number of suicide attempts (SA), (including intentional overdoses and intentional self-harm) in the acute phase: 62 events in 59 patients, 40 events in 39 patients on SSRIs, 20 events in 18 patients on placebo and two events in two patients on imipramine

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on the suicide attempts
HMAI	Dec. 1993	Jan. 1996	MDD	8 weeks Study had 1week (5-7 days) LI and responders entered a EXT/CONT phase	DLX 5mg	**No patient details available, at v5** Suicide attempt This event was only listed in the appendix within the tables for all adverse events for all patients. The event was "suicide attempt" at visit 5, mild for a different patient and not considered a SAE. No further details are available from the CSR.
HMAI	Dec. 1993	Jan. 1996	MDD	8 weeks Study had 1week (5-7 days) LI and responders entered a EXT/CONT phase	DLX 5mg	**No patient details available, at v4** Suicide attempt This event was listed both in the SAE table in the main report, in the appendix within the tables for all adverse events for all patients. The event was "suicide attempt" at visit 4, severe and led to discontinuation. No further details are available from the CSR.
HMAI	Dec. 1993	Jan. 1996	MDD	8 weeks Study had 1week (5-7 days) LI and responders entered a EXT/CONT phase	DLX 20mg	**No patient details available, at v12** Suicide attempt This event was listed both in the SAE table in the main report, in the appendix within the tables for all adverse events for all patients. The event was "suicide attempt" at visit 12, severe and led to discontinuation. No further details are available from the CSR.
HMAI	Dec. 1993	Jan. 1996	MDD	8 weeks Study had 1week (5-7 days) LI and responders entered a EXT/CONT phase	DLX 5mg	**No patient details available, at v4** Intentional overdose This event was listed both in the SAE table in the main report, in the appendix within the tables for all adverse events for all patients. The event was "suicide attempt" at visit 12, severe and led to discontinuation. No further details are available from the CSR.
HMAI	Dec. 1993	Jan. 1996	MDD	8 weeks Study had 1week (5-7 days) LI and responders entered a EXT/CONT phase	DLX 20mg	**No patient details available, at v8 and v9 (2 events)** Intentional overdose This event was listed both in the SAE table in the main report, in the appendix within the tables for all adverse events for all patients. The event was "suicide attempt" at visit 12, severe and led to

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on the suicide attempts
						discontinuation. No further details are available from the CSR.
HMAI	Dec. 1993	Jan. 1996	MDD	8 weeks Study had 1week (5-7 days) LI and responders entered a EXT/CONT phase	PLB	**No patient details available, at v6** Suicide attempt This event was only listed in the appendix within the tables for all adverse events for all patients. The event was "suicide attempt" at visit 6, severe for a PLB patient and considered severe and led to discontinuation. No further details are available from the CSR.
HMAI	Dec. 1993	Jan. 1996	MDD	44 weeks EXT/ CONT This was the continuation phase after the 8 week main randomised phase.	DLX 5mg	**No patient details available, at v17** Suicide attempt This event was listed both in the SAE table in the main report, in the appendix within the tables for all adverse events for all patients. The event was "suicide attempt" at visit 17, severe and led to discontinuation. No further details are available from the CSR.
HMAI	Dec. 1993	Jan. 1996	MDD	44 weeks EXT/ CONT This was the continuation phase after the 8 week main randomised phase.	DLX 10mg	**No patient details available, at v14** Suicide attempt This event was listed both in the SAE table in the main report, in the appendix within the tables for all adverse events for all patients. The event was "suicide attempt" at visit 14, severe but did not led to discontinuation. No further details are available from the CSR.
HMAI	Dec. 1993	Jan. 1996	MDD	44 weeks EXT/ CONT This was the continuation phase after the 8 week main randomised phase.	PLB	**No patient details available, at v16** Intentional injury This event was only listed in the appendix within the tables for all adverse events for all patients. The event was "intentional injury" at visit 16, severe for a PLB patient and considered severe but did not led to discontinuation. No further details are available from the CSR.
X065	April 1991	Feb. 1995	MDD paediatric	8 weeks Study had 1-2 weeks LI and no LO phase	FLX 20mg	**16Y F patient, at v5 on day15** Intentional overdose on tablets of Pamprin, 6 tablets of Momentum, and 15 tablets of Dibromm "*...patient had fight with boyfriend went home and took 8 tablets of Pamprin, 6 tablets of Momentum, and 15 tablets of Dibromm. Patient was taken to emergency room ...by mother.....Patient discontinued from the study. Other AE listed as: manic reaction, insomnia, nausea, nervousness, pallor, and somnolence."*

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on the suicide attempts
X065	April 1991	Feb. 1995	MDD paediatric	8 weeks Study had 1-2 weeks LI and no LO phase	FLX 20mg	**17Y F patient, at v4 on day 12** Intentional overdose on unknown pills but possibly Ibuprofen and Phenegran **"...***patient made a suicide attempt and went to the Emergency Room. The suicide attempt was done with unknown pills, possibly Ibuprofen and 4 Phenegran tablets. At the Emergency Room, patient was given activated charcoal with sorbital of 50 gms. Patient was then discharged and sent home. Patient continued in the study and completed the protocol. Other AE listed as: Anxiety, depression, hyperkinesia, migraine, neurosis, thinking abnormal, abdominal pain, asthenia, menstrual disorder, nausea and dysrnenorrhea."*
HCJE	April 1998	July 2000	MDD paediatric	9 weeks Study had 1week PLB LI phase and no LO phase*	FLX Dose unknown	**No patient details available, days on therapy unknown** Intentional Injury (mild) This event was only noted within the adverse events table and no narrative was available
HCJE	April 1998	July 2000	MDD paediatric	9 weeks Study had 1week PLB LI phase and no LO phase*	PLB	**15Y M patient, on day 37** Intentional injury *"...This patient with a prior history of self-mutilatory behaviour was randomized to placebo treatment on 22-December-1998. Patient was hospitalized for suicidal ideation and self-mutilatory behaviour on 28- January-1999. Investigator discontinued patient from study due to this condition. The patient had 37 days of study drug therapy at the time of discontinuation ....Other adverse events included suicidal ideation and homicidal ideation".*
HCJW	March 1999	Aug. 2000	OCD paediatric	13 weeks Study had no PLB LI phase and no LO phase	FLX 20mg	**12YF patient, on day 25/28** Intentional Overdose on acetaminophen *"...The patient received study drug beginning 23-June-1999 and received last dose on 20-July-1999. On 17-Jul-1999, the patient took approximately 20 acetominophen 500mg tablets during a suicide attempt. She experienced nausea and vomiting but did not notify her mother of the overdose until 19-July-1999. Her mother then took her to an urgent care center and labs were drawn. The patient came in for visit 6 on 20- Jul-1999 but neither the mother or the patient told the site about the incident. She was admitted to the hospital on 20-Jul-1999 for elevated liver enzymes. The mother*

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on the suicide attempts
						called the investigator on 21-Jul-1999 to report the hospitalization. The patient was discharged from the hospital on 23-Jul-1999..." Two different sections within the CSR noted this incident as occurring on day 25 or on day 28 and the event was noted as "elevated liver enzymes", within the adverse event tables (which was the consequence of the SA).
HCJW	March 1999	Aug. 2000	OCD paediatric	13 weeks Study had no PLB LI phase and no LO phase	FLX Dose unknown	**7Y to 13Y F patient, day unknown** Intentional Injury (moderate) This event was only noted within the adverse events table and no narrative was available and only age group (not actual age) available.
HCJW	March 1999	Aug. 2000	OCD paediatric	13 weeks Study had no PLB LI phase and no LO phase	PLB	**13Y to 18Y F patient, day unknown** Intentional Injury (mild) This event was only noted within the adverse events table and no narrative was available and only age group (not actual age) available.
627	July 1998	Jan. 2000	PTSD	12 weeks Study had a 7 days PLB LI and up to 3 weeks of taper LO phase.	PAR 20mg	**27Y M patient, on day 4** Intentional Overdose on unknown tablets (possibly Lasamet). *"...The patient received oral study medication, paroxetine 20mg, 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 was withdrawn from the study on 05 September 1998....."*
377	April 1995	May 1998	MDD paediatric	12 weeks Study had 2 weeks PLB LI and 2 weeks of taper LO phase.	PAR 20mg	**18/ 17Y F patient, on day 79/80** Intentional Overdose on PAR **"....***On 7 March 1997, the patient received her first treatment with study medication for depression. Approximately eighty days later, on 25 May 1997, the patient attempted suicide using an overdose of*

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on the suicide attempts
						study medication. The patient was hospitalised but was given no treatment medication as there were no signs or symptoms associated with the overdose. Study medication was discontinued on 25 May 1997..." The age of this same patient and event was noted as 17 years and 18 years and event date as 79 days and 80 days in two different places in the CSR.
377	April 1995	May 1998	MDD paediatric	12 weeks Study had 2 weeks PLB LI and 2 weeks of taper LO phase.	PAR 75mg	**17Y F patient, on day 74/75** Intentional Overdose on PAR **".....***On 7 November 1995, the patient received her first treatment with study medication for depression. Approximately seventy five days later, on 20 January 1996, the patient took an intentional overdose of 28 tablets of study medication. The patient stated that she took the overdose because she felt nervous and was not attempting suicide. ...The patient was hospitalised ....and study medication was discontinued on 20 January 1996. The only sign of the overdose was a mild tremor of the upper extremities..."* The event date is noted as 74 days and 75 days in two different places in the CSR.
377	April 1995	May 1998	MDD paediatric	12 weeks Study had 2 weeks PLB LI and 2 weeks of taper LO phase.	PAR 30mg	**16Y F patient, on day 69** Intentional Overdose on PAR *"...On 13 November 1997, the patient received her first treatment with study medication for major unipolar depression. Approximately sixty nine days later, on 19 January 1998 at 16:00 hours, the patient took an overdose of six capsules of study medication. The overdose was considered an "impulsive act" and accidental. The patient was not hospitalised and reported no adverse reactions as a result of the overdose. Study medication was not discontinued. The most recent information received on 20 January 1998 reports that the patient has fully recovered. ...other possible etiological factors include the fact that the patient had an argument with her mother."*
377	April 1995	May 1998	MDD paediatric	12 weeks Study had 2 weeks PLB LI and 2 weeks of taper LO phase.	PAR 20mg	**14Y F patient, on day 53/54** Self-harm and suicide attempt by superficial cuts in the left wrist **"...***At the time of the event, the patient was suffering from postprandial abdominal pain and headache. On 17 December 1997, the patient received her first treatment with study medication*

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on the suicide attempts
						for unipolar major depression. Approximately fifty four days later, on 8 February 1998, the patient attempted suicide after arguing with her mother concerning her decision to marry another man. The patient locked herself in the bathroom and made superficial cuts in her left wrist using a shaving blade. She stated that she did not want to live at the moment, feeling anguish and anger. This episode of crisis lasted approximately two hours, after which the patient calmed and "absorbed" the idea of self destruction. ...Study medication was not interrupted; it was increased. Both the investigator and SB monitor wished for the patient to continue the study under strict supervision....but later was withdrawn due to protocol violation." The incident was noted as 'Emotional Lability/Suicide Attempt' in the narrative and only as emotional lability within the tables and the day of event was listed as 53 or 54 days in different sections of the CSR.
377	April 1995	May 1998	MDD paediatric	12 weeks Study had 2 weeks PLB LI and 2 weeks of taper LO phase.	PAR 20mg	**15Y F patient, on day 16** Intentional overdose – not stated on what mediction. *".. On day 7 the patient experienced agitation and anxiety lasting 16 days. The investigator considered the experiences to be severe and related to study medication. The patient was on 20mg paroxetine when the adverse experience started. Study drug was stopped on Day 13, and other corrective therapy was given for insomnia, but three days later the patient experienced emotional lability leading to an intentional overdose...."*
377	April 1995	May 1998	MDD paediatric	12 weeks Study had 2 weeks PLB LI and 2 weeks of taper LO phase.	PLB	**14Y F patient, on day 31** Intentional overdose on clorazepate and PLB *"..On 14 October 1995, the patient received her first treatment with study medication for unipolar major depression. Approximately thirty one days later, on 13 November 1995, the patient attempted suicide by taking an overdose of study medication with Tranxene (clorazepate) [28 x 20mg study medication and 7 capsules clorazepate, dose not specified]. The patient was withdrawn from the study the same day due to protocol violation..."*
377	April 1995	May 1998	MDD paediatric	12 weeks Study had 2 weeks	PLB	**15Y F patient, on day 83** Intentional overdose on alprazolam

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on the suicide attempts
				PLB LI and 2 weeks of taper LO phase.		*"On 29 February 1996, the patient received her first treatment with study medication for unipolar major depression. Approximately eighty three days later on 21 May 1996, the patient took an intentional overdose of the benzodiazipine, Xanax (alprazolam) (21 tablets). The following day she appeared more tired than usual and, after telling her mother what she had done, was taken to hospital. No treatment was required and the patient was discharged the same day.....Study medication was discontinued on 21 May 1996..."*
377	April 1995	May 1998	MDD paediatric	12 weeks Study had 2 weeks PLB LI and 2 weeks of taper LO phase.	PLB	**17Y F patient, on day 30** Suicide attempt and self-harm by pair of scissors and cigarette lighter. *"....On 6 March 1996, the patient received her first treatment with study medication for depression. Approximately thirty days later, on 4 April 1996, the patient attempted suicide using a pair of scissors, after visiting her mother and being molested by her brother. She stopped when her mother came into the room. The wound was not serious. She has also tried to burn herself with a cigarette lighter. These self-damaging acts were ongoing at the time of reporting. Study medication was discontinued on 1 May 1996. The patient was withdrawn from the study and referred for psychotherapy...."*
701	March 2000	Jan. 2001	MDD paediatric	8 weeks Study had no PLB LI phase and up to 4 weeks of taper LO phase.	PAR 50mg	**16Y F patient, on day 42** Intentional overdose on PAR *"The patient received the first dose of study medication on 05 May 2000. The patient began treatment at a dose of 10 mg/day and was titrated up, in 10 mg/week increments, to the highest dose of 50 mg on 01June2000. On 14-Jun-2000, the patient received the last dose of study medication. She withdrew from the study that day due to lack of efficacy. The patient claimed to have ingested 100 tablets of the taper study medication at 9:30 PM on 15 June 2000, after a fight with her mother. At 4:30 AM the next morning (16 June 2000), the patient informed her mother, who then brought the patient to an emergency room. The patient reportedly felt "shaky" since 1:00 AM. The emergency room doctor stated that the patient "looked okay," but was "slightly tachycardic" with a pulse of 100. The patient was also slightly diaphoretic, with a blood pressure of*

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on the suicide attempts
						140/104. ...A urine drug screen was administered, which was found to be negative for approximately 700 compounds including paroxetine and other "antidepressants." The drug screen was positive for caffeine. The patient was referred to an inpatient psychiatric unit...."
701	March 2000	Jan. 2001	MDD paediatric	8 weeks Study had no PLB LI phase and up to 4 weeks of taper LO phase.	PAR 30mg	**11Y M patient, on day 31** Suicide threat with a knife to wrist *"....The patient began receiving treatment with study medication on 10-October-2000. The patient began treatment at a dose of 10 mg/day and was titrated up to the highest dose of 30 mg on 24 October 2000. The patient received the last dose of study medication on 06 November 2000 (Day 28). No reason was given for cessation of medication. On 08-Nov-2000 (Day 30), two days later, the patient held a knife to his wrist and threatened to harm himself. The patient was hospitalized with an acute exacerbation of major depressive disorder. The patient was treated with Wellbutrin® (amfebutamone hydrochloride), and was discharged in stable condition. The event was reported to be resolved on 13-Nov-2000. The patient was withdrawn from the study due to the event...."* This event was listed as 'Acute exacerbation of major depressive disorder [depression aggravated] within the adverse event tables and was only noted as a preparatory SA on reading the patient narrative.
701	March 2000	Jan. 2001	MDD paediatric	8 weeks Study had no PLB LI phase and up to 4 weeks of taper LO phase.	PAR 30mg	**10Y F patient, on day 19** Suicide attempt by smothering with pillows **"....***The patient began treatment at a dose of 10 mg/day and was titrated up, in 10 mg/week increments, to the highest dose of 30 mg on 27 October 2000. The last dose of study medication was taken on 02 November 2000 (Day 20). On 02-Nov-2000 (Day 20), 19 days after the first dose, the patient was hospitalized after a 5-day history of extreme uncontrolled aggression. The patient had been getting "out of control," with acts of aggression and violence. The patient tried to smother herself with pillows in the hospital examination room. The patient was diagnosed with exacerbation of symptoms of major depressive disorder. Treatment with study*

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on the suicide attempts
						medication was stopped due to this event, and the patient was withdrawn from the study...."
676	Nov. 1999	Oct. 2001	SAD/SP paediatric	16 weeks Study had no PLB LI phase and up to 4 weeks of taper LO phase.	PAR 20mg	**16Y F patient, on day 38** Self-harm of scratch on right wrist *"...The patient received the first dose of study medication on 17 October 2000 at dose level 1 (10 mg/day), which was increased to dose level 2 (20 mg/day) on 22 November 2000. The last dose of study medication was taken on 28 November 2000 (Day 43). On 21 October 2000 (Day 5), mild lack of emotion was reported. On 23 November 2000 (Day 38), mild emotional lability (self-inflicted scratch on right wrist) was reported. This condition abated in one day without corrective therapy, and was considered to be probably unrelated to treatment with study medication. On 28 November 2000 (Day 43), moderately severe depression (worsening depression) was reported..... and the patient was withdrawn from the study. No taper medication was dispensed, but Paxil® (paroxetine) 20 mg per day was prescribed to treat the worsening depression..."*. The event was noted as 'Depression (Worsening Depression)' in the CSR.
329	April 1994	Feb. 1998	MDD paediatric	8 weeks Study had no PLB LI phase and no LO phase**	PAR 20mg	**14Y F patient, on day 13/14** Intentional overdose on Tylenol *"..On 28-Mar-96, the patient received her first dose of study medication. On 10-April-96, the patient had overdosed on Tylenol. She had ingested 27 or 28 capsules in response to being grounded and was taken into an emergency room for her stomach to be pumped. She was released and scheduled for follow-up liver function test. On 14-April-96, the patient was withdrawn from the study...."* The CSR noted the event as Emotional lability (Tylenol overdose intentional/asymptomatic) in the narrative and as emotional lability in the adverse event tables. Date of event was noted as day 13 in one place and day 14 in another in the CSR.
329	April 1994	Feb. 1998	MDD paediatric	8 weeks Study had no PLB LI phase and no LO phase**	PAR 40mg	**15Y F patient, on day 37** Intentional overdose on PAR *"....On 14-Mar-96, the patient received her first dose of study medication. The patient exceeded compliance from 19-April-96 through 09-May-96. The overdose was rated by the investigator as*

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on the suicide attempts
						serious, moderate in intensity ...the patient continued in the study and completed the acute phase ...on 09-May-96...”
329	April 1994	Feb. 1998	MDD paediatric	8 weeks Study had no PLB LI phase and no LO phase**	PAR 20mg	**18Y M patient, on day 12** Self-harm with superficial cuts and suicide attempt planned by jumping off the roof *On l 7-May-96, the patient received his first dose of study medication. On 28-May-96, the patient was hospitalized for psychosis with auditory hallucinations and superficial cuts. A voice commanded him to hurt himself. All the cuts closed without medical attention. The voice also commanded the patient to jump from the roof. Although the patient went to the roof he did not jump. It was determined that the patient was a risk to himself. Study medication was discontinued on admission. ....”*
329	April 1994	Feb. 1998	MDD paediatric	8 weeks Study had no PLB LI phase and no LO phase**	PAR 20mg	**15Y F patient, on day 57** Intentional overdose on PAR and multiple other drugs (Advil, Ibuprofen, Tylenol, fiorinal and unknown white pills) *“... On 15-Feb-95, the patient received her first dose of study medication. She completed the week 7 visit of the acute phase on 05-Apr-97. Following a disagreement with her mother, on 12-Apr-95, the patient intentionally overdosed. She consumed 12 tablets of study drug (level 4), 23 Advil, 12 Ibuprofen 400's, 23 Ibuprofen 600's, 29 "long skinny white pills", 4 Tylenol's and 10 fiorinal tablets. The patient reported headache, constipation, myalgia, myasthenia, and dizziness. The patient was withdrawn from the study on 12-Apr- 95, prior to completion of the final study visit....”*
329	April 1994	Feb. 1998	MDD paediatric	8 weeks Study had no PLB LI phase and no LO phase**	IMI 200mg	**13Y F patient, on day 31** Self-mutilation *“...The patient received her first dose and last dose of study medication on the 30-August-1996 and 12-0ctober-1996, respectively. On the 29-Septermber-1996, the patient experienced depression and self mutilation for which she was hospitalized. ..In the evening of the Ol-October-96, the patient started down level titration at level 3. Then on the 12-0ctober-96, she decided to stop taking study medication and she eventually withdrew from the study on the 16-0ctober-96....”*

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on the suicide attempts
93ce21 -0640	May 1994	March 1996	PTSD	12 weeks Study had 1week PLB LI phase and no LO phase	SER 25mg/day	**39Y F patient on day 4** Intentional Overdose on SER *"The patient had a history of physical and sexual assault and grew increasingly symptomatic after an encounter with a previous assailant. She had been on 25 mg sertraline daily from 10/24 - 10/26/95, and on 10/27/97 ingested 425 mg sertraline (17 tablets) in an effort to obtain symptomatic relief. She suffered no sequelae of the overdose, and returned to the study site for her visit on 10/31/96 at which time it was determined that she had decompensated, and she was discontinued from the study ..."*
93ce21 -0640	May 1994	March 1996	PTSD	12 weeks Study had 1week PLB LI phase and no LO phase	PLB	**33Y F patient, on day 10** Self-harmful behaviour (mild aggressive reaction) *"Mild aggressive reaction (self-harmful behaviour), depersonalization, and emotional lability of 1-2 days duration, all resolving by the day of the last dose. Investigator felt latter two were pre-existing Axis II traits not noted at screening. Patient claimed history of self-harmful behaviour, not reported at screening."* Patient was discontinued from the study and moderate anxiety was also noted.
86CE2 1-0238	May 1987	May 1989	MDD	8 weeks Study had 1week PLB LI phase and 2 weeks (week 9 and 10) of taper LO.	SER 50mg	**33Y F patient, on day 7** Intentional Overdose on SER *"Patient ...was discontinued after 7 days of double-blind therapy as the result of a suicide attempt in which she ingested 27 capsules of study medication (3 capsules of sertraline 50 mg[=150 mg total and 24 capsules of placebo). The patient was not hospitalized, but reported headache and diarrhoea tor 2 days subsequent to the event..."*
86CE2 1-0238	May 1987	May 1989	MDD	8 weeks Study had 1week PLB LI phase and 2 weeks (week 9 and 10) of taper LO.	PLB	**29/30Y F patient, on day 49** Intentional Overdose on chloral hydrate and beer *"Patient ...was discontinued after 55 days of double-blind medication after ingestion of 5 quarts of beer and 15,000 mg of chloral hydrate in a suicide attempt. The patient was hospitalized and received treatment...."* The event was coded as a suicide attempt occurred on day 4. The patient's was listed as 29 and as 30 years in two different tables.

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on the suicide attempts
A0501 001	Dec. 1999	May 2001	MDD paediatric	10 weeks Study had no PLB LI phase and no LO phase	SER 100mg	**10Y F patient, on days 35-49** Suicidal treat with a kitchen knife to the neck *"The subject developed increasing suicidal ideation with a plan, beginning on 12 March 2001, 35 days after beginning sertraline. The subject was treated with sertraline 25 mg/day from 06-08 February 2001, 50 mg/day from 09 - 27 February 2001, and was taking 100 mg/day of sertraline from 28 February 2001 up to the onset of the event. Reportedly, the subject held a kitchen knife to her neck while alone but did not cut herself. She was scheduled for a study visit on 19 March 2001 and reported the suicidality, at which point she was hospitalized and discontinued permanently from the study. ..."* The event was noted as suicidal ideation with a plan.
A0501 017	Feb. 2000	March 2001	MDD paediatric	10 weeks Study had no PLB LI phase and no LO phase	SER 150mg	**16Y F patient, on day 48/50** Intentional Overdose on multiple drugs **"...***the subject attempted suicide by multi-drug overdose. The subject was involved in a family argument regarding school attendance.....She was hospitalized and study drug was permanently discontinued. The subject ingested unknown quantities of ibuprofen, Naprozen, aspirin, acetaminophen/pseudoephedrine, brompheniramine/pseudoephedrine, and dimenhydrinate...."* The event was coded as a severe suicide attempt and noted as occurring on 48 days of therapy in one table (discontinuations), and on day 50 in the SAE table for the same event and patient.
A0501 017	Feb. 2000	March 2001	MDD paediatric	10 weeks Study had no PLB LI phase and no LO phase	SER 100mg	**6Y M patient, on day 34** Suicide attempt by threatening to jump out of a moving vehicle *"Sertraline was administered orally from 08 October 2000 until 10 November 2000, a total of 34 days. Total daily dose at onset of event was 100 mg. On 10 November 2000, the subject attempted suicide by threatening to jump from a moving vehicle stating that he wanted to kill himself. Later that same evening he expressed suicidal ideation and was hospitalized. Events that may have affected the subject were: 1) his grandmother attempted suicide 2 weeks earlier and 2) his mother informed him that he was going to be withdrawn from the study and that he was to start psychotherapy..."*

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on the suicide attempts
A0501 017	Feb. 2000	March 2001	MDD paediatric	10 weeks Study had no PLB LI phase and no LO phase	PLB	**17 Y F patient, on day 14** Suicide attempt by immolation *"Placebo was administered orally from 18 January 2001 to 31 January 2001. On 26 January 2001, on the ninth day of study drug, the subject attempted suicide by immolation. Her siblings doused the flames immediately. She was left with minor burns on her abdomen and one on her left shoulder that were treated with topical antibiotics. The subject admitted that she was angry with her parents for going away and leaving her alone at home, because she was fearful. The subject admitted that she had acted impulsively and had not intended to kill herself. The subject's parents did not report this event until 01 February 2001 because they felt the subject's burns were small and she was recovering. Placebo was permanently discontinued on 01 February 2001 due to insufficient clinical response, and she was started on sertraline (50 mg/day). The subject was administered chlorpromazine for sedation. There was no evidence of psychosis or clear premeditation leading to the event..."*
A0501 017	Feb. 2000	March 2001	MDD paediatric	10 weeks Study had no PLB LI phase and no LO phase	PLB	**16Y F patient, on 62 days and 66 days (2 events)** Suicide attempt by hanging and then overdose attempt with PLB One event noted as post study event in CSR *"Placebo was administered orally from 21 November 2000 to 25 January 2001, a total of 66 days. On the subject's last study visit (end of week 10), the investigator was informed that the subject had attempted suicide twice: on 22 January 2001, after an argument with her brother, she tried to hang herself and was prevented from doing so by her family. Three days later, on 25 January 2001 she consumed 32 tablets of study drug. She suffered no side effects following consumption of placebo tablets but was hospitalized for suicidal ideation and further management. The suicidal ideation resolved on 03 February 2001, but the subject continued to remain in the hospital for social reasons. The subject was considered to have completed study treatment and the event was coded in AEM as a post-therapy event. The subject had no relevant history or other illnesses present at the onset of the event. No known concomitant therapy was taken..."*

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on the suicide attempts
88CE21-0371 & 88CE21-0372	Dates unknown	Dates unknown	OCD	12 weeks Study had 1 week PLB LI phase and completers continued in a EXT/CONT phase	SER 200mg/day	**No patient details available, days on therapy unknown** Suicide attempts (1 severe) This event was only noted within the adverse events table and no narrative or further was available.
88CE21-0371 & 88CE21-0372	Dates unknown	Dates unknown	OCD	48 weeks This was the EXT/ CONT part of the study and had a 4 weeks of taper LO phase	SER 200mg/day	**No patient details available, days on therapy unknown** Suicide attempts (1 moderate) This event was only noted within the adverse events table and no narrative or further was available.
050-310	Dates redacted	maybe May 1988	MDD	4 weeks Study had 7-14 days PLB LI phase and no LO phase	SER 100mg	**No patient details available, days on therapy unknown** Suicide attempt *"One patient …sertraline 100mg), received one capsule of amitriptyline following a suicide attempt on of the double-blind treatment period. Thereafter, the patient returned to double-blind medication as scheduled. No data have been excluded from any analyses as a result of this occurrence."* The event was only obtained in the section related to the deviations from the protocol (due to the use of AMY an excluded medication). The CSR had a table in the appendix on 'Incidence or side effects (all causalities)', but no suicide attempt was listed there and unclear what it was coded as.
050-310	Dates redacted	maybe May 1988	MDD	4 weeks Study had 7-14 days PLB LI phase and no LO phase	SER 200mg	**No patient details available, days on therapy unknown** Suicide attempt The table listing the reasons for discontinuation have noted 1 suicide attempt for 200mg that led to discontinuation, but no narrative is available for us. The following section which may have relevant details have been redacted (blackened) and the subsequent pages "*removed due to confidential patient information*".
050-310	Dates redacted	maybe May 1988	MDD	4 weeks Study had 7-14 days PLB LI phase and no LO phase	PLB	**No patient details available, days on therapy unknown** Suicide attempt by intoxification **(2 events noted)** The table listing the reasons for discontinuation and main report text reporting on discontinuations state that

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on the suicide attempts
						"...patient in the placebo group, a (redacted text) year old discontinued after (redacted text) of treatment having had inadequate response and making two suicidal at tempts ("intoxication" on both occasions)."
050-334	Feb. 1992	Feb. 1993	MDD or bipolar depresson	6 weeks The trial had a 4 to 14 days of PLB LI and no LO phase***	PLB	**41 Y F patient, on day 12** Intentional overdose on centrally acting drugs *"....She had suffered 5 episodes of depression over the previous 11 years but had never attempted suicide before. She was receiving prazepam until her suicide attempt on Day 12 and had been treated with clomipramine until one week before the study...."*
050-334	Feb. 1992	Feb. 1993	MDD or bipolar depresson	6 weeks The trial had a 4 to 14 days of PLB LI and no LO phase***	PLB	**37Y F patient, on day 37** Suicide attempt, no further details **"....***a 37 year old female was classed as markedly ill on entering the study after 3 weeks of depression.... She had not been given antidepressants during this episode but had been taking* ***diazepam*** *until 8 days before her suicide attempt on Day 37, when it was replaced with a combination of aceprometazine/ meprobamate. She had suffered 10 episodes of depression over the previous 24 years and had attempted suicide on 5 occasions."*
0600B-367-EU	Oct. 1994	Sept. 1995	MDD	8 weeks Study had a 7 ± 10 days PLB LI and up to 3 days of taper LO phase.	PAR 20mg	**64Y M patient, on day 43** Intentional Overdose on paracetamol and vodka *"..The current episode of depression started in July 1994 when his wife died. He had taken an overdose of meptaxinol (4 tablets of 200 mg) on November 3, 1994. He was randomly assigned to receive paroxetine on November 22, 1994. ...and the patient was not suicidal. ...Over the Christmas holidays, he began to miss his wife and started to drink. On January 3, he drank 2/3 of a bottle of vodka and ingested approximately 50 tablets of paracetamol (500 mg). He was hospitalized and ...was discharged on January 5, 1995 with a treatment of Seroxat 20 mg..."*
0600B-367-EU	Oct. 1994	Sept. 1995	MDD	8 weeks Study had a 7 ± 10 days PLB LI and up to 3 days of taper LO phase.	PAR 20mg	**37Y M patient, on 38** Intentional Overdose on sulphasalazine, propranolol and zolpidem (doses unknown) and alcohol. *"...He had a childhood history of behavioral problems, including rages, and had taken an overdose in 1982. The present episode of*

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on the suicide attempts
						depression was considered to be his first and had started in June 1994. He was randomly assigned to receive paroxetine on December 22, 1994. There is some doubt whether he took study medication from January 7 until January 28. On January 28, the patient was hospitalized for an overdose with sulphasalazine, propranolol and zolpidem (doses unknown) and alcohol. No study medication was taken in the overdose. The patient was discharged from hospital on January 29 after the treatment code was broken..."
0600B-367-EU	Oct. 1994	Sept. 1995	MDD	8 weeks Study had a 7 ± 10 days PLB LI and up to 3 days of taper LO phase.	VEN ER 150 mg	**42Y M patient, on day 41** Self-harm (mild alcoholic intoxication) *"....He was randomly assigned to venlafaxine ER 150 mg/day on May 24, 1995. ...After temporary improvement of the depression, the patient relapsed (associated with mild alcohol intoxication) and was hospitalized from July 3 to July 19. During hospitalization a mild confusion and dissociative disorder (de-realization) were observed. Patient was discharged with good improvement. .. The patient discontinued the study on July 3...."*
0600B 1-384-US/EU /CA	Sept. 1997	Nov. 1999	MDD	6 weeks The trial had a 7 ± 4 days of PLB LI planned but was not followed strictly. The LO varied as well****	VEN ER Dose unknown	**42Y M patient, on day 3** Suicide attempt with a kitchen knife **"***On 05 September 1999, the patient attempted to injure himself with a kitchen knife. The patient was hospitalized. As of 20 Sept 99, his condition had stabilized and he had no suicidal tendencies. He remained hospitalized for treatment of depression. No other information is available on this patient."*
0600B 1-384-US/EU /CA	Sept. 1997	Nov. 1999	MDD	6 weeks The trial had a 7 ± 4 days of PLB LI planned but was not followed strictly. The LO varied as well****	IMI 125mg	**18Y M patient, on day 34.** Intentional Injury by cutting wrist *"On 05 December 1998, the patient intentionally cut his wrist. He was inebriated and disappointed in a love affair. The wounds were dressed and he was hospitalized in a psychiatric ward until 07 December1998."*
0600B 1-384-US/EU /CA	Sept. 1997	Nov. 1999	MDD	6 weeks The trial had a 7 ± 4 days of PLB LI	PLB	**40Y F patient, on day 25/29** Intentional overdose on sleeping pills *"On 14 September 1998, the patient phoned the investigational site*

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on the suicide attempts
				planned but was not followed strictly. The LO varied as well****		*and reported that she had taken "a bunch of sleeping pills" during the weekend of 29 Auust1998 in a suicide attempt. No treatment was noted." The day of event was noted as 25 in adverse event tables and 29 in the narrative."*
0600B 1-384-US/EU /CA	Sept. 1997	Nov. 1999	MDD	6 weeks The trial had a 7 ± 4 days of PLB LI planned but was not followed strictly. The LO varied as well****	PLB	**40Y M patient, on day 17** Intentional overdose on PAR and Ibuprofen *"....On 08 October 98, the patient presented to an emergency room having reportedly taken 2 handfuls each of ibuprofen and paroxetine and 3 or 4 tablets of study drug.....The patient remained lucid throughout the event and had no sequelae. He was hospitalized until 30 Oct ober1998. He was discharged on paroxetine.*
0600B 1-384-US/EU /CA	Sept. 1997	Nov. 1999	MDD	6 weeks The trial had a 7 ± 4 days of PLB LI planned but was not followed strictly. The LO varied as well****	PLB	**73Y F patient on day 36** Suicide attempt by stabbing at heart with a knife **"***On 25 March 1998, the patient stabbed herself below the heart with a pocket knife. The wound was 2 cm deep, with no signs of pleural or cardiac damage. The patient was treated surgically. Study drug was discontinued. After the event, the patient was described as well and stable."*
600A-:302-US, CA/302	July 1988	Aug. 1990	MDD	6 weeks The trial had a 7 ± 3 days of PLB LI and up to 6 days of taper LO	PLB	**19Y F patient, on day 5** Intentional overdose on unknown medication **"..***19-year-old woman in placebo arm took an intentional overdose of mother's medication on day 5. There was no history of suicidal ideation at entry into this trial, but 2-3 years earlier the patient had overdosed herself with "half a bottle" of Midol (medication for the relief of premenstrual syndrome)..."*

DLX: duloxetine; FLX: fluoxetine; IMI: imipramine; PAR: paroxetine; PLB: placebo; VEN: venaflaxine; VEN ER: venlafaxine extended release

FPFV: first patient, first visit; LPLV: last patient last visit; LI: lead-in phase of trial; LO: lead-out phase of the trial; EXT/ CONT: extension phase of the trial

Aug.: August; Jan: January; Dec.: December; Feb.: February; F: female; M: male; MDD: major depressive disorder; Nov.: November; OCD: obsessive compulsive disorder; Oct.: October; PT: post therapy; PTSD: posttraumatic stress disorder; Sept.: September; v: visit number; Y: years

*The HCJE FLX trial had a 9 week acute randomised phase (Study Period III and Study Period IV, where Study Period III was a double-blind adaptation period that lasted for 1 week and patients were randomized to receive either FLX 10 mg/day or PLB; and Study Period IV was a double-blind, fixed-dose acute treatment period that lasted for 8 weeks and patients were to FLX received 20 mg/day during this period or PLB). This was followed by an EXT/CONT phases: subchronic treatment phase and relapse prevention phase (Study Period V and Study Period VI, where Study Period V was a double-blind, non-responder re-randomization period that lasted for 10 weeks, responders at Visit 10 remained on fluoxetine 20 mg/day or PLB and FLX non-responders were re-randomized to either remain on FLX 20 mg/day or to receive fluoxetine 40 mg/day with an option to titrate to 60 mg/day. PLB non-responders remained on PLB; and Study Period VI was a double-blind, relapse prevention period that lasted for 32 weeks. FLX responders were re-randomized to either continue on the current FLX dose or PLB. PLB responders remained on PLB.
** The 329 PAR trial had no LO phase but clinical responders had treatment for 6 months with monthly visits. The non responders at the end of the 8-week study were withdrawn from the study and treated in an open-label manner.
*** There was no LO phase but patients who experienced a clinically significant improvement in their depressive syndrome were to be entered into a continuation study (Protocol 334C) with maintenance of their double blind medication for an additional 20 weeks. We did not have access to data from this phase of the study.
****The 0600B 1-384-US/EU/CA results state that PLB LI was for 3-11 days but 1 patient is listed as having only 1 day of LI. The LO planned was tapering of dose for 3 weeks, but only 1 week for Europe, however taper phase could be omitted or adjusted (up to 21 days in US and CA; 10 days in EU) if medically indicated. Data from 4-10 days after therapy was also noted.

Supplementary data Table 7 Number of suicide attempts (SA), (including intentional overdoses and intentional self-harm) in the lead-out or post therapy phase: 5 events in 5 patients, three on SSRIs (two on paroxetine and one on venlafaxine) and two on placebo.

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on the suicide attempts
701	March 2000	Jan. 2001	MDD paediatric	8 weeks Study had no PLB LI phase and up to 4 weeks of taper LO phase.	PAR 30mg	**15Y F patient, on day 53, 2 days after last dose** Suicide attempt by cutting open arm and intentional overdose on different Tylenol medications *"..The patient began receiving treatment with study medication on 28-April-2000. The patient began treatment at a dose of 10 mg/day and was titrated up, in 10 mg/week increments, to the highest dose of 30 mg on 18 May 2000. On l 7- June-2000 (Day 51), the patient*

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on the suicide attempts
						received the last dose of study medication. On l 9- Jun-2000 (Day 53), two days after the last dose, the patient took 12 Extra Strength Tylenol® (paracetamol) and half a bottle of Tylenol Cold® tablets (chlorpheniramine/pseudoephedrine HCl/ dextromethorphan/ acetaminophen), and she also cut open her arm. The patient was hospitalized, placed in an intensive care unit, and underwent a stomach lavage. The patient was expected to be transferred to a psychiatric hospital. The patient was found to have low potassium and hemoglobin values. Treatment included prescription Paxil® (paroxetine/dose unknown), trazodone, and an iron supplement. The patient was considered withdrawn from the study because of this event. The overdose was reported to have resolved on l 9-Jun-2000, and the arm lacerations was reported to have resolved in Jul-2000...."
377	April 1995	May 1998	MDD paediatric	12 weeks Study had 2 weeks PLB LI and 2 weeks of taper LO phase.	PLB	**14 Y F patient, on day 87 (during taper phase)** Intentional overdose on paracetamol *"...On 18 December 1997, the patient received her first treatment with study medication for depression. Approximately eighty seven days later, on 14 March 1998, the patient attempted suicide by the ingestion of paracetamol tablets (20 x 500mg) and was hospitalised.....and study medication was discontinued on 24 March 1998 at visit 10. The patient was reported to have recovered on 14 March 1998, but at the time of reporting, she remained hospitalised. ...the patient had just started the down titration phase of the study...."*
0600B-367-EU	Oct. 1994	Sept. 1995	MDD	8 weeks Study had a 7 ± 10 days PLB LI and up to 3 days of taper LO phase.	PAR 20mg	**40Y F patient, 6 days after last dose** Intentional overdose on alprazolam *"...The current episode had started in September 1994. She was randomly assigned to receive paroxetine on April 15, 1995..... The patient took her last active dose of study medication on June 10, 1995, and completed the study on June 15....On June 2, she took 10 tablets of alprazolam 0.25 mg as a suicidal gesture. No specific action was taken.*
0600B-367-EU	Oct. 1994	Sept. 1995	MDD	8 weeks Study had a 7 ± 10 days PLB LI and up	PLB	**38Y F patient, 10 days after last dose** Intentional overdose on zolpidem **"...***The current episode started in March 1995. She was randomly*

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on the suicide attempts
				to 3 days of taper LO phase.		*assigned to receive placebo on May 25 1995..... The patient completed the study on July 23 1995. Her mood began to change on July 26 (Study day 63) related to a background of a sentimental break up. After visit 8 on August 2, she reported a suicide attempt by swallowing 10 tablets of Stilnox (IE 100 mg zolpidem). She was hospitalized on August 6 and was discharged on August 18 under Deroxat treatment...."*
0600B 1-384-US/EU /CA	Sept. 1997	Nov. 1999	MDD	6 weeks The trial had a 7 ± 4 days of PLB LI planned but was not followed strictly. The LO varied as well****	VEN ER 210mg	**55Y M patient, 20 days after last dose** Intentional overdose on PAR *"On 20 August19 99, the patient took an overdose of 20, 20 mg paroxetine tablets. He was evaluated at a hospital and was not considered at risk from the overdose. Neither intervention nor hospitalization were needed. The patient was considered much improved when seen 2 weeks later as an outpatient.* The patient discontinued from study after 4 days on VEN ER therapy for reasons other than AE 8not stated what exactly), and the event occurred 20 days after last dose. This patient is only mentioned in the narratives, not the serious adverse event table listings or anywhere else in the CSR.

PAR: paroxetine; PLB: placebo; VEN: venaflaxine; VEN ER: venlafaxine extended release
FPFV: first patient, first visit; LPLV: last patient last visit; LI: lead-in phase of trial; LO: lead-out phase of the trial; EXT/ CONT: extension phase of the trial
Jan: January; F: female; M: male; MDD: major depressive disorder; Nov.: November; Oct.: October; PT: post therapy; Sept.: September; v: visit number; Y: years

Supplementary data Table 8 Number of suicidal ideation (SI) events in the pre-randomisation: 6 events in 6 patients, four events on duloxetine and two events on placebo

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on suicidal ideation
HMBC	March 2002	July 2003	MDD	26 weeks Study had an open label single arm LI phase with DLX prior randomisation and a 12 weeks rescue phase with either DLX 60 once daily or twice daily	DLX open label 60mg/ day	**49Y F patient, at v8 on day 75 (for 5 days)** Suicidal ideation (severe) ***"..... St****arted on open label duloxetine 60 mg QD, experienced the serious adverse event of suicidal ideation. The patient was started on open label duloxetine 60 mg QD on 9 October 2002. Upon screening the patient denied any alcohol abuse or dependence. On 22 December 2002 the patient called 911 as she had been drinking heavily. She was hospitalized in the inpatient mental health unit for suicidal ideation. ...She stated that 11 she wanted to drink herself into oblivion and didn't care if she ever woke up or not". ..She was discharged on 26-Dec-02. On 3 January 2003 the patient completed the open label phase of the study and was randomized to duloxetine 60 mg...".*
HMBC	March 2002	July 2003	MDD	26 weeks Study had an open label single arm LI phase with DLX prior randomisation and a 12 weeks rescue phase with either DLX 60 once daily or twice daily	DLX open label 60mg/ day	**24Y M patient, at v6 day on 45 (for 5 days) - Actual Term** Suicidal ideation (severe) *"...Started treatment on 2 July 2002. On 14 August 2002, the patient called the investigator to report a situational crisis due to family conflict. An emergency appointment was scheduled for 15 August 20 02. But in the early morning hours of 15 August the patient was hospitalized for suicidal ideation. The patient permanently discontinued study drug on this date. The patient's last dose of study drug was 14 August 2002....."*
HMBC	March 2002	July 2003	MDD	26 weeks Study had an open label single arm LI phase with DLX prior randomisation and a 12 weeks rescue phase with either DLX 60 once daily or twice daily	DLX open label 60mg/ day	**No patient details available, at v8 (exact day unknown)** Suicidal ideation (mild) The treatment emergent adverse event tables and serious adverse event tables within the main report listed 3 events of SI (for which narratives were available) and one mild event (for which no narrative and therefore no details were available). One mild SI event was noted at v8 from the appendix of all line listings of adverse events for all patients.
HMBC	March	July	MDD	26 weeks	DLX	**No patient details available, at v1 (exact day unknown)**

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on suicidal ideation
	2002	2003		Study had an open label single arm LI phase with DLX prior randomisation and a 12 weeks rescue phase with either DLX 60 once daily or twice daily	open label 60mg/ day	Suicidal thoughts (mild) The treatment emergent adverse event tables and serious adverse event tables within the main report listed 3 events of SI (for which narratives were available) and one mild event (for which no narrative and therefore no details were available). One event of mild suicidal thoughts was additionally noted event was noted at v1 for a different patient, from the appendix of all line listings of adverse events for all patients.
HMBOa	July 2001	March 2002	FM with or without MDD	1 week Study had 12 weeks acute randomised phase and no LO phase	PLB LI	**51Y F patient, at v1 (exact day unknown)** Suicidal thoughts (serious) *"....was not randomized to study drug in the study, experienced the serious adverse event of suicide risk due to major depressive disorder. The principal investigator considered the serious adverse event of suicide ideation as life threatening ....The patient came in for visit 1 on 06 December 2001. After performing part of the MINI, the patient was discontinued from the study due to high suicide risk. ...The principal investigator spoke with patient's personal physician. The personal physician requested that the patient be sent to the emergency room immediately for evaluation and follow-up. ..."*
HCJE	April 1998	July 2000	MDD paediatric	1 week PLB LI Study had 9 weeks acute randomised phase and no phase LO phase**	PLB LI	**16Y M patient, after v2 on day 2 of study** Suicidal thoughts (serious) *".....discontinued the study due to clinical findings of suicidal ideation, and was exclusionary according to protocol requirements. ....Patient was in the evaluation phase of the study and was hospitalized on 27-December-1998 for suicidal ideation. This event occurred after visit 2 but prior to the scheduled visit 3. Investigator discontinued patient from the study due to the serious suicidal risk, which is protocol exclusion number 20. ....Investigator discontinued patient from the study due to the serious suicidal risk...."*

DLX: duloxetine; PLB: placebo;
FPFV: first patient, first visit; LPLV: last patient last visit; LI: lead-in phase of trial; LO: lead-out phase of the trial
F: female; FM: Fibromyalgia; M: male; MDD: major depressive disorder; PT: post therapy; v: visit number; Y: years

* There were 533 patients on DLX for 12 weeks open label and this was followed by a total of 278 patients who continued the study and were randomised at v8 to either receive PLB (142) or DLX (136) for a further 26 weeks.
**The HCJE FLX trial had a 9 week acute randomised phase (Study Period III and Study Period IV, where Study Period III was a double-blind adaptation period that lasted for 1 week and patients were randomized to receive either FLX 10 mg/day or PLB; and Study Period IV was a double-blind, fixed-dose acute treatment period that lasted for 8 weeks and patients were to FLX received 20 mg/day during this period or PLB). This was followed by an EXT/CONT phases: subchronic treatment phase and relapse prevention phase (Study Period V and Study Period VI, where Study Period V was a double-blind, non-responder re-randomization period that lasted for 10 weeks, responders at Visit 10 remained on fluoxetine 20 mg/day or PLB and FLX non-responders were re-randomized to either remain on FLX 20 mg/day or to receive fluoxetine 40 mg/day with an option to titrate to 60 mg/day. PLB non-responders remained on PLB; and Study Period VI was a double-blind, relapse prevention period that lasted for 32 weeks. FLX responders were re-randomized to either continue on the current FLX dose or PLB. PLB responders remained on PLB

Supplementary data Table 9 Number of suicidal ideation (SI) events in the acute randomised phase: 63 in 62 patients,

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on suicidal ideation
HMBHa	Nov. 2000	May 2001	MDD	9 weeks The study had a merged screening and a gradual PLB LI (flexible time) phase and a gradual taper LO (flexible time) phase up to 2 weeks	DLX 60mg	**No patient details available, at v6 (exact day unknown)** Suicidal ideation (moderate) This event was not listed in any treatment emergent adverse event tables nor in the main text of the report and was only noted from the appendix of all line listings of adverse events for all patients.
HMBHa	Nov. 2000	May 2001	MDD	9 weeks The study had a merged screening and a gradual PLB LI (flexible time) phase and a gradual taper LO (flexible time) phase up to 2 weeks	DLX 60mg	**No patient details available, at v6-v9 (exact days unknown)** Suicidal ideation (moderate) This event was not listed in any treatment emergent adverse event tables nor in the main text of the report and was only noted from the appendix of all line listings of adverse events for all patients.

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on suicidal ideation
HMBHa	Nov. 2000	May 2001	MDD	9 weeks The study had a merged screening and a gradual PLB LI (flexible time) phase and a gradual taper LO (flexible time) phase up to 2 weeks	DLX Dose unknown	**No patient details available, at v4 (exact day unknown)** Increased suicidality (moderate) This event was not listed in any treatment emergent adverse event tables nor in the main text of the report and was only noted from the appendix of all line listings of adverse events for all patients.
HMBHb	Nov. 2000	May 2001	MDD	9 weeks The study had a merged screening and a gradual PLB LI (flexible time) phase and a gradual taper LO (flexible time) phase up to 2 weeks	DLX 60mg	**No patient details available, at v6 (exact day unknown)** Fleeting suicidal thoughts (moderate) This event was not listed in any treatment emergent adverse event tables nor in the main text of the report and was only noted from the appendix of all line listings of adverse events for all patients.
HMBHb	Nov. 2000	May 2001	MDD	9 weeks The study had a merged screening and a gradual PLB LI (flexible time) phase and a gradual taper LO (flexible time) phase up to 2 weeks	PLB	**No patient details available, at v1, v2-v6 (exact days unknown)** Thoughts of suicide (mild to moderate) This event was not listed in any treatment emergent adverse event tables nor in the main text of the report and was only noted from the appendix of all line listings of adverse events for all patients.
HMBHb	Nov. 2000	May 2001	MDD	9 weeks The study had a merged screening and a gradual PLB LI (flexible time) phase and a gradual taper LO (flexible time) phase up to 2 weeks	PLB	**No patient details available, at v1, v4-v8 (exact days unknown)** Occasional suicidal thoughts (moderate) This event was not listed in any treatment emergent adverse event tables nor in the main text of the report and was only noted from the appendix of all line listings of adverse events for all patients.
HMBHb	Nov. 2000	May 2001	MDD	9 weeks The study had a	PLB	**No patient details available, at v1, v4-v5 (exact days unknown)** Suicidal ideation (mild to moderate)

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on suicidal ideation
				merged screening and a gradual PLB LI (flexible time) phase and a gradual taper LO (flexible time) phase up to 2 weeks		This event was not listed in any treatment emergent adverse event tables nor in the main text of the report and was only noted from the appendix of all line listings of adverse events for all patients.
HMAYb	Oct. 2000	Jan. 2003	MDD	26 weeks This was the EXT/CONT phase of the trial after a 8 week acute phase with a 2 week PLB LO period	DLX 60mg	**32Y F patient, at v9 on day 77** Suicidal ideation (serious) *".....discontinued from the study due to the serious adverse event of worsening of depression on 3-May-2001, 84 days after randomization to duloxetine 60 mg BID for depression. The patient had one previous episode of major depression from June through August of 2000. The current episode of depression started in November of2000. The patient entered the study on 25-January 200l. The patient first reported worsening of depression on 26-April 200 I, 77 days after randomization. On 3-May-2001, the patient was hospitalized for the worsening of depressive symptoms. .....The patient's mood was reportedly labile but the depression improved and suicidal ideations disappeared during hospitalization. Last dose of duloxetine was 3-May-01, 84 days after randomization to blinded therapy.* This event was listed as 'worsening of depression' in the adverse event tables and the SI was only noted by the patient narrative, as it noted that "*suicidal ideations disappeared during hospitalization*", indicating that they existed before.
HMATa	March 2000	April 2001	MDD	8 weeks The study had a 1 week PLB LI and a 2 weeks PLB LO	DLX 20mg	**21Y F patient, at v4-v6 on day 6** Suicidal ideation (severe) **".....**discontinued from the study on 12-January-2001, 17 days after randomization to Duloxetine 20 mg BID, due to the adverse event of dissociation. The patient experienced an increasing sense of dissociative feelings for 5 days prior to discontinuation (dissociative feelings began 12 days after randomization) ....**S**evere suicidal urges began on 01- January-2001, 6 days after randomization, and continued through discontinuation. The patient stated that the dissociative feelings contributed to her suicidal thoughts....." No suicidal ideation was noted in tables and only in

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on suicidal ideation
						the patient narratives and the appendix of all line listings of adverse events for all patients.
HMATa	March 2000	April 2001	MDD	8 weeks The study had a 1 week PLB LI and a 2 weeks PLB LO	PAR 20mg	**No patient details available, at v6 (exact days unknown)** Suicidal ideation (mild) This event was not listed in any treatment emergent adverse event tables nor in the main text of the report and was only noted from the appendix of all line listings of adverse events for all patients.
HMATb	March 2000	Feb. 2001	MDD	8 weeks The study had a 1 week PLB LI and a 2 weeks PLB LO	PAR 20mg	**No patient details available, at v6 exact day unknown** Suicidal Ideation **(**moderate) This event was not listed in any treatment emergent adverse event tables nor in the main text of the report and was only noted from the appendix of all line listings of adverse events for all patients.
HMBC	March 2002	July 2003	MDD	26 weeks Study had an open label single arm LI phase with DLX prior randomisation and a 12 weeks rescue phase with either DLX 60 once daily or twice daily	DLX 60mg	**25Y F patient, at v13 on day 51** Threatened to harm oneself with a knife *"...On 22-Nov-02, 51 days after starting duloxetine (in R phase, or day 140 for 4 days), the patient experienced auditory hallucinations, increased depressive symptoms, and made suicidal threats. Early that AM, the patient threatened to harm herself while in the possession of a knife. The patient's partner reported that the patient had an increase in depressive symptoms due to psychosocial stressors that included loss of a job, denial of a loan application, and arguments with her family and partner. The patient was admitted to the hospital.....The patient reported her last dose of study drug was on 17-November-2002. On 25-Nov-02 the patient was discharged from hospital. The adverse event of suicide threats resolved by 26-November-2002 and increased depressive symptoms resolved on 7-December-2002 but the event of auditory hallucination was still on-going at the patients last visit on 10-December 2002. The patient was discontinued from the trial on 10-December 2002 due to protocol violation."*
HCJE	April 1998	July 2000	MDD paediatric	9 weeks Study had 1 week PLB LI and no phase LO phase**	FLX 20mg	**13.26Y F patient, on day 70** Increased suicidal ideation *"..Parent (mother) phoned site to report patient was hospitalized on 12-April-1999 for suicidal ideation. Patient had a history of suicidal ideation with an onset of 8-November-1998, prior to study*

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on suicidal ideation
						entry. Investigator decided to discontinue patient from study due to an increase in the patient's suicidal ideation. ....Patient had 70 days of study drug therapy at the time of discontinuation."
Protocol 377	April 1995	May 1998	MDD paediatric	12 weeks Study had 2 weeks PLB LI and 2 weeks of taper LO phase.	PAR Dose unknown	**17Y F patient, on day 56** Suicidal risk "....experienced emotional lability and worsening depression and was considered a suicide risk. It lasted 25 days.."
Protocol 377	April 1995	May 1998	MDD paediatric	12 weeks Study had 2 weeks PLB LI and 2 weeks of taper LO phase.	PAR Dose unknown	**15Y F, on day 23** Parasuicidal "...experienced emotional lability and was parasuicidal for one day"
Protocol 377	April 1995	May 1998	MDD paediatric	12 weeks Study had 2 weeks PLB LI and 2 weeks of taper LO phase.	PAR	**17Y M patient, on day 37** Suicidal intent "...On day 35 experienced severe irritability and nervousness considered possibly related to study drug. This was followed on day 37 by severe emotional lability with suicidal intent...."
Protocol 627	July 1998	Jan. 2000	PTSD	12 weeks Study had a 7 days PLB LI and up to 3 weeks of taper LO phase.	PLB	**34Y M patient, day 14** Suicidal ideation *"The patient received oral study medication (placebo dose level 1) from 22 September 1999. On Day 6 (27 September 1999), the patient experienced dizziness, lightheadedness, dyspepsia, insomnia and nausea (all moderate in intensity) all lasting 2 days except for the insomnia which continued beyond the end of the study, which all resulted in discontinuation of the study medication. The patient was withdrawn from the study the same day due to dyspepsia. ...No corrective therapy was given for these events. On 05 October 1999, some 8 days after the last dose, the patient experienced major depression including insomnia, loss of appetite, anergia, amotivation, diminished concentration, severe agitation, a sense of hopelessness and helplessness and suicidal ideation. The patient was reported not to have attempted suicide nor have a definite plan for the future. The patient was verbally aggressive on admission due to an alcoholic binge. According to the patient's wife he had*

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on suicidal ideation
						been drinking heavily prior to his admission and was suffering from alcohol abuse, he had been verbally abusive and threatening towards her. ...”
Protocol 627	July 1998	Jan. 2000	PTSD	12 weeks Study had a 7 days PLB LI and up to 3 weeks of taper LO phase.	PLB	**29 Y Fpatient, on day 4** Suicidal ideation “*....The patient received oral study medication (placebo dose level 1) from 12 March 1999. Prior to the study the patient had experienced moderate worsening of depression (04 March 1999) lasting 5 days, moderate restlessness on 09 March 1999) which continued beyond the end of the study and moderate sleeplessness on 12 March 1999 which also continued beyond the end of the study. On 15 March 1999, four days after the first dose the patient developed a suicidal i*deation*. The patient refused to eat or drink and became socially withdrawn. ....Treatment with study medication was stopped due to the suicidal ideation on 15 March 1999 and the patient was withdrawn from the study the same day....”*
Protocol 627	July 1998	Jan. 2000	PTSD	12 weeks Study had a 7 days PLB LI and up to 3 weeks of taper LO phase.	PLB	**45Y M patient, on day 1** Suicidal ideation (mild) *“.....Concomitant medications included chloral hydrate from 18 June 1999 to 20 June 1999 for insomnia....The patient received study medication on 17 June 1999. The same day the patient experienced increased depression, tearfullness and mild suicidal ideation. The patient was hospitalised on 22 June 1999. ...Treatment with study medication was stopped due to a protocol violation on 17 June 1999....”*

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on suicidal ideation
Protocol 701	March 2000	Jan. 2001	MDD paediatric	8 weeks Study had no PLB LI phase and up to 4 weeks of taper LO phase.	PAR 20mg	**11Y F patient, on day 20** Suicidal ideation *"...The patient began treatment with study medication on 06-September 2000. The patient began treatment at a dose of 10 mg/day and was titrated up to the highest dose of 20 mg on 13 September 2000. The last dose of blinded study medication was taken on 21 September 2000. On 25-Sep-2000 (Day 20), 19 days after the first dose, and 4 days after the last dose of study medication, the patient's mother called the investigator site to report that her daughter was admitted to the hospital for suicidal ideation. The patient had stated to her mother that she wanted to hang herself from the ceiling fan. The patient's mother thought that daughter was "attention seeking." No action was reportedly taken in regard to this event, but the patient was lost to follow-up...."*
Protocol 701	March 2000	Jan. 2001	MDD paediatric	8 weeks Study had no PLB LI phase and up to 4 weeks of taper LO phase.	PLB	**13 Y M patient, on day 5** Suicidality *"....The patient began therapy with study medication on 21-June-2000. On 26-June- 2000, 5 days later, the patient stole his parent's car and "wrecked it," and was hospitalized due to suicidal ideation. On 30-June-2000, the event was reported as resolved, and the patient was discharged from the hospital. It was reported that the patient was placed in a juvenile detention center. Treatment with study medication was stopped due to this event, and the patient was withdrawn from the study...."* This event was listed as a suicide attempt due to coding dictionary limitations in certain sections of the CSR for the verbatim term, but coded as emotional lability in the adverse event tables which was the preferred term in the coding dictionary.
Protocol 676	Nov. 1999	Oct. 2001	SAD/SP paediatric	16 weeks Study had no PLB LI phase and up to 4 weeks of taper LO phase.	PAR 40mg	**13Y F patient, on day 30** Suicidal thoughts *".....The patient received the first dose of study medication on 30 August 2000. The patient began treatment at dose level 1 (10 mg/day). The dose was increased to dose level 2 (20 mg/day) on 13 September 2000, to dose level 3 (30 mg/day) on 19 September*

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on suicidal ideation
						2000, and to dose level 4 (40 mg/day) on 25 September, 2000, which continued throughout the remainder of the study. The last dose of study medication was taken on 02 October 2000 (Day 34). On 10 September 2000 (Day 12), the patient reported moderately severe myalgia (muscle discomfort), which was treated with ibuprofen and Tylenol® (paracetamol) and resolved in three days. The dose of study medication was increased in response to this condition. This event was considered to be unrelated to treatment with study medication. On 14 September, 2000 (Day 16), moderately severe agitation (panic attack) was reported. This cleared without treatment in one day and was considered to be probably unrelated to treatment with study medication. On 28 September 2000 (Day 30), the patient experienced severe agitation (panic attack worsening) lasting one day, which was considered by the investigator to be possibly related to treatment with study medication, and severely intense abnormal dreams (morbid thoughts) that were considered to be probably unrelated to treatment with study medication. In addition, moderately severe emotional lability (suicidal thoughts) was also reported to have begun on this date...."
Protocol 704	Jan. 2000	July 2001	OCD paediatric	10 weeks The study had no LI phase but up to 4 weeks taper LO phase	PAR 40mg	**15Y M patient, on day 25 (for 8 days)** Suicidal thoughts *"....On Day 25 of study medication, 1 day after reaching his maximum dose level, the patient began to have suicidal thoughts (preferred term: emotional lability) while staying at a youth shelter. He was hospitalized for evaluation, and, as a result of this event, study medication was stopped. ..."*
Protocol 329	April 1994	Feb. 1998	MDD paediatric	8 weeks Study had no PLB LI phase and no LO phase**	PAR 20mg	**14Y M patient, on day 14** Possible suicide thoughts *"....On l 7-November-1994, the patient received his first dose of study medication. On 30-November1994, the patient became very angry. He punched pictures, broke glass, and sustained lacerations that required six sutures. His anger subsided, but he expressed hopelessness and possible suicide thoughts. The patient was hospitalized due to his severe anger outburst and a worsening of his depression. ....Study medication was discontinued on this day...."*

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on suicidal ideation
Protocol 329	April 1994	Feb. 1998	MDD paediatric	8 weeks Study had no PLB LI phase and no LO phase**	PAR 20mg	**14Y F patient, about 56 days** Saying one would kill oneself *".....On 07-March-1995, the patient received her first dose of study medication. As reported by the site, the patient began exhibiting symptoms of disinhibition, grandiosity, and expansive mood at around week four of the study. A clinical judgement was made by site medical staff to observe the patients behavior for the next one to two weeks for diagnostic and intervention planning. ...On 04-April 1995, the patient reported increased feelings of elation and expansive mood. There was also a decreased need for sleep, increased energy and an inflated self esteem. Other symptoms included accelerated speech, flight of ideas, motor hyperactivity. The school reported impulsive and sexually provocative behavior. Her behavior was closely monitored. On 02-May 95, the patient became agitated and said she would kill herself following threats of punishment from her mother to control her behavior. The patient was deemed a risk to herself and was brought to the crisis service. She was hospitalized on 02-May-95 and the decision was made that she would not enter the continuation phase...."*
Protocol 329	April 1994	Feb. 1998	MDD paediatric	8 weeks Study had no PLB LI phase and no LO phase**	PAR 20mg	**16Y F patient, on day 37** Suicidal ideation *"On 23-January-1997, the patient received her first dose of study medication. On 24-February-1997, the patient became more isolative, sleeping more and not attending to school. The study medication was discontinued on 24-February-1997 by the patient's mother without the knowledge of the study investigator or coordinator. The patient started Prozac the following day. Four days later, on 28-February1997, the patient did not sleep well all night, cried and experienced suicidal intentions. She was subsequently hospitalized for severe suicidal ideation..."* At the time of the SI event, the patient was on FLX rather than PAR.
Protocol 329	April 1994	Feb. 1998	MDD paediatric	8 weeks Study had no PLB LI phase and no LO phase**	IMI 200mg	**15Y F patient, on day 32** Suicidal ideation (moderate) *".....was randomized to imipramine 50mg/day on 30-January-1995. Dose was up-titrated to 200mg/day in 50mg/week increments*

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on suicidal ideation
						by week 4. Study medication was stopped on day 32 because of suicidal ideation with gesture considered to be of moderate severity. ..."
Protocol 329	April 1994	Feb. 1998	MDD paediatric	8 weeks Study had no PLB LI phase and no LO phase**	PLB	**16/17 Y F patient, about 6 weeks** Suicidal thoughts *"....She commenced study medication on 04-January-1996. Approximately 6 weeks after commencing study 329, the patient experienced severe worsening of depression with severe suicidal thoughts. ....Study drug was stopped on 21-February-1996. The investigator reported that the worsening of depression and suicidal thought were life threatening ...Patient has a history of suicidal ideation without a definite plan. She has never had a suicide attempt..."* This event was coded as emotional lability (preferred term) in the adverse event tables.
Protocol 648	Feb. 1999	Feb. 2000	PTSD	12 weeks Study had 1 week LI and 2-3 weeks double blind tapering LO with a 2 week follow up PT	PAR Dose unknown	**37Y M patient, about 22 days** Suicidal thoughts *".....entered R phase on 29-September-1999 & approx. 22 days later, on 21-October-1999, the patient was hospitalized with depression and suicidal thoughts. Study medication was discontinued on 21-October-1999 & the patient was started on Prozac (fluoxetine)..."* This event was coded as depression and emotional lability (preferred term) in the adverse event tables.
Protocol 651	Feb. 1999	Jan. 2000	PTSD	12 weeks Study had 1 week LI and 2 weeks of taper LO	PAR 40mg	**38Y F patient, on day 15** Suicidal Ideation "*....The patient's medical history includes a suicide attempt in August 1998 .....On 14-July-1999, the patient began treatment with blinded study medication for post traumatic stress disorder. Fourteen days later, on 28-July-1999, the patient had a routine study visit. At that time, the patient reported a recent breakup of a long-term relationship. The patient denied suicidal ideation at that time. The following day, on 29-Jul-1999, the patient was brought to the hospital by the county sheriff for suicidal ideation and for property damage. The patient was hospitalized for a 24 hour involuntary hold for observation. Treatment with study medication was stopped due to this event on 28-July-1999....."*. No listing of suicidal ideations in main report. The event was coded as emotional

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on suicidal ideation
						lability (preferred term) in adverse event tables and the verbatim term in the narrative was suicide attempt, due to the dictionary.
Protocol 651	Feb. 1999	Jan. 2000	PTSD	12 weeks Study had 1 week LI and 2 weeks of taper LO	PAR 40mg	**46Y F patient, on day 26** Suicidal ideation/urges with a plan *"This case refers to a 46-year-old female ....Concomitant medications include chloral hydrate, cimetidine and loratadine. The patient took double-blind study medication for posttraumatic stress disorder from 25-Jun-1999 until 18-July-1999. The patient completed visit 4 with good compliance, and insomnia as an adverse event (non-serious). She did not keep her visit 5 appointment and was contacted by phone. She said that on 18-July-1999, she discontinued study medication due to persistent insomnia and anxiety. (Chloral hydrate had been helpful for sleep, but she had stopped it on 15-July-1999). On 20-July-1999, two days after stopping study medication, the patient consumed excessive alcohol, and while intoxicated, called a friend and asked if he would help her load a gun so she could kill herself as her PTSD symptoms were overwhelming. The friend stayed with her through the night, and she was without suicidal ideation/urges by the following day. The patient was seen on 05-Aug- 1999 for a termination visit and related the above story. She reported that she felt more anxious both on the study medication and for about one week after stopping it ....The event resolved by 21-Jul-1999."*
Protocol 651	Feb. 1999	Jan. 2000	PTSD	12 weeks Study had 1 week LI and 2 weeks of taper LO	PLB	**28Y F patient, about 54 days** Suicidal Ideation *".....On 24-March-1999, the patient began treatment with double-blind study medication for post traumatic stress disorder. Subsequently, the patient was involved in a pedestrian - automobile accident in which she was the pedestrian. Two days prior to her accident, she was fired from her job. After the accident, the patient reported an increase in anxiety, decreased self-worth, increase in intrusive thoughts about the accident and suicidal ideation. On 17-May-1999, 54 days after receiving the first dose of blinded study medication, the patient was evaluated and hospitalized in the medical-psychiatry unit. Study medication was discontinued on 16-May-1999....."*
R -	May	March	PTSD	12 weeks	SER	**27Y F patient, day unknown**

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on suicidal ideation
93ce21-0640	1994	1996		Study had 1week PLB LI phase and no LO phase	Dose unknown	Suicidal Ideation This event was only noted in the all adverse event listings and no further information is available as there was no patient narrative.
R - 93ce21-0640	May 1994	March 1996	PTSD	12 weeks Study had 1week PLB LI phase and no LO phase	PLB	**40Y F patient, day unknown** Suicidal Ideation This event was only noted in the all adverse event listings and no further information is available as there was no patient narrative.
R - 93ce21-0640	May 1994	March 1996	PTSD	12 weeks Study had 1week PLB LI phase and no LO phase	PLB	**27Y F patient, day unknown** Suicidal Ideation This event was only noted in the all adverse event listings and no further information is available as there was no patient narrative.
R-93CE21-0641	May 1994	Sept. 1996	PTSD	12 weeks Study had 1week PLB LI phase and no LO phase	SER 25mg	**46 Y M patient, day 6** Suicidal Ideation *"....suicidal ideation, severe ....discontinued....resulting in hospitalization and resolving with treatment 7 days after last dose. Attributed to fiancée calling off marriage after finding out about subject's past."*
R-93CE21-0641	May 1994	Sept. 1996	PTSD	12 weeks Study had 1week PLB LI phase and no LO phase	SER Dose unknown	**29 Y F patient,** Suicidal Ideation (mild) This event was only noted in the all adverse event listings and no further information is available as there was no patient narrative.
R-93CE21-0641	May 1994	Sept. 1996	PTSD	12 weeks Study had 1week PLB LI phase and no LO phase	SER Dose unknown	**37 F patient, about 87 days** Suicidal Ideation (mild) This event was only noted in the all adverse event listings and no further information is available as there was no patient narrative.
R-93CE21-0641	May 1994	Sept. 1996	PTSD	12 weeks Study had 1week PLB LI phase and no LO phase	PLB	**30 Y F patient, on day 20** Suicidal Ideation (severe) This event was only noted in the all adverse event listings and no further information is available as there was no patient narrative. This patient also reported severe depersonalization.
R-93CE21-	May 1994	Sept. 1996	PTSD	12 weeks	PLB	**47 Y M patient, on day 43** Suicidal Ideation

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on suicidal ideation
0641				Study had 1week PLB LI phase and no LO phase		"*..Started acute phase on 5th July 1994 and on 7/5/94 was upset because his check had not come and because of a meeting with other veterans. He mentioned suicidal ideation to a worker at the subject's homeless shelter and was sent to the emergency room. He was admitted to the hospital, where he denied suicidal intent. He was released from the hospital after three days, and completed the study on 8/15/94*"
R-93CE21-0641	May 1994	Sept. 1996	PTSD	12 weeks Study had 1week PLB LI phase and no LO phase	PLB	**51 Y M patient, on day 8** Suicidal Ideation (mild) This event was only noted in the all adverse event listings and no further information is available as there was no patient narrative. The patient continued and completed the study.
90CE21-0498	Dates unknown	Dates unknown	OCD paediatric	12 weeks Study had 1week PLB LI phase and no LO phase	PLB	**No details available on patient, day unknown** Suicidal Ideation (mild) This event was only noted in the treatment emergent adverse event tables and no further information is available on this event.
R-0601	Jan. 2000	May 2001	GSP	12 weeks Study had 7 to 14 days of PLB LI phase and up to 2 weeks of taper LO phase	SER Dose unknown	**No details available on patient, day unknown** Suicidal Ideation (mild) This event was only noted in the treatment emergent adverse event tables and no further information is available on this event.
050-336	Nov. 1992	Sept. 1994	OCD	12 weeks Study had 7 to 14 days of PLB LI phase and no LO phase	SER 50mg	**36 Y F patient on day 7** Potentially suicidal "*....patient experienced mood swings and was potentially suicidal...other adverse events include: apathy, emotional lability, fatigue..*"
STL-NY-94-004	March 1996	Oct. 1997	SP	20 weeks Study had 1week PLB LI phase and unclear whether any LO or drug free period exits, but some could enter an EXT	PLB	**50 Y M patient, on days 126-140 and still present on last day of follow-up** Suicidal Ideation (moderate) This event was only noted in the all adverse event listings and no further information is available as there was no patient narrative.

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on suicidal ideation
				trial		
93CE21-0629	April 1994	April 1995	PD	10 weeks Study had 2weeks PLB LI phase and no LO phase	PLB	**No age available , F patient, day unknown** Suicidal Ideation (mild) This event was only noted in the treatment emergent adverse event tables and no further information is available on this event.
A0501001	Dec. 1999	May 2001	MDD paediatric	10 weeks Study had no PLB LI phase and no LO phase	SER 50 mg	**10Y M patient, on days 21-26** Suicidal ideation "*....Twenty-one days after starting sertraline, on 09 November 2000, he was involved in an argument with his teacher and he made a comment suggestive to the teacher of suicidality. The school social worker was not immediately available to assess the child so ...the subject hospitalized. His attending physician saw no evidence of suicidality and he was discharged from the hospital on 14 November 2000. The subject was permanently discontinued from the study....*"
A0501001	Dec. 1999	May 2001	MDD paediatric	10 weeks Study had no PLB LI phase and no LO phase	SER 100mg	**12Y M patient, on days 56-62** Suicidal ideation "*....The subject developed worsening symptoms of major depressive disorder on 12 July 2000 and expressed suicidal ideation on 19 July 2000. Because the subject could not contract for safety, the investigator decided to hospitalize the subject. Duration of sertraline therapy up to the event was 55 days. The subject was taking 100 mg/day of sertraline at the time of the event. The subject has a past psychiatric history of suicidal ideation. ... He was taking no concomitant medications prior to the event. The subject was permanently discontinued from the study due to worsening of the subject's major depressive disorder....*"
237/248 (80ce21-0237 and 86ce21-0248)	Dates unknown	Dates unknown	OCD	8 weeks The study had a 1 week PLB LI phase and a 2 week taper LO phase	PLB	**No details on patient available, on day 26** Suicidal ideation (severe) "*Patient .....experienced severe suicidal ideation after 26 days of placebo treatment. This event is classified as "suicide attempt" according to WHO terminology.... although an actual gesture or attempt did not occur. The patient was discontinued from the study 4 days after onset of suicidal ideation, although the investigator discontinued the patient due to "insufficient, clinical response"*

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on suicidal ideation
						rather than any adverse experience. The suicidal ideation resolved 6 days after study discontinuation (10 days after onset) and has not recurred..."
371/372 SHORT (88CE21-0371/ 0372 (12 weeks)	Dates unknown	Dates unknown	OCD	12 weeks Study had 1 week PLB LI phase and completers continued in a EXT/CONT phase	SER 200mg	**33Y M patient, on day 78** Suicidal ideation (severe) *"...severe suicidal ideation secondary to acute depression....Patient hospitalized. Suicidal ideation resolved after 1 day's duration. Patient had history of depression pre-dating study* This event was listed as inter-current illness rather than within the adverse events tables.
600A-313-US	May 1989	June 1990	MDD	6 weeks	VEN 25mg	**19YM patient, on day 21** Suicidal ideation "*..A 19-year-old man was enrolled on July 19, 1989, with a 34-week history of major depression and anxiety attacks. He had suicidal thoughts prior to enrolment. He was randomly assigned to treatment with venlafaxine 25 mg/d and showed some improvement. However, he was withdrawn prematurely on day 22 (August 9, 1989) because the depression returned. The depression, including suicidal ideation, was similar to that seen at the pre-study evaluation....*" This event was noted as depression in the adverse event tables and only noted as depression with suicidal ideation from the patient narrative.
600A-313-US	May 1989	June 1990	MDD	6 weeks The study had a 7 ± 3 days of PLB LI and within 72 hours of completion, patients could elect to enrol in an EXT trial (protocol 600A-314-US)	PLB	**35Y F patient, on day 7** Suicidal thoughts *"...This 35-year-old woman enrolled on April 26, 1990. She had a history of 2 suicide attempts, in 1967 and in the mid-1970s, as well as current suicidal ideation. She was randomly assigned to placebo but was withdrawn 7 days later because of worsening of the depression and increasing suicidal thoughts...."* This event was noted as worsened depression in the adverse event tables and only noted as depression with suicidal ideation from the patient narrative.
0600B-367-EU	Oct. 1994	Sept. 1995	MDD	8 weeks The study had a 7 ± 10 days f PLB LI and	VEN ER 150mg	**42Y F patient, on day 58** Suicidal obsessions (severe) This event was only noted in the all adverse event listings and no

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on suicidal ideation
				up to 3 days of taper LO phase		further information is available as there was no patient narrative.
0600B-367-EU	Oct. 1994	Sept. 1995	MDD	8 weeks The study had a 7 ± 10 days f PLB LI and up to 3 days of taper LO phase	PAR 20mg	**58Y M patient**, **on day 29**, Anxiety/suicidal thoughts *"...This 58-year-old male patient was screened for suitability for the study on February 16, 1995 and was randomly assigned to receive paroxetine on February 23, 1995..... On March 23... the patient was admitted to hospital. He presented with severe psychomotor retardation with disruption of diurnal/nocturnal patterns and with severe anxiety, feelings of worthless and suicidal thoughts.....The patient was discontinued from the study at the time of hospitalization on March 23..."*
0600B 1-384-US/EU/ CA	Sept. 1997	Nov. 1999	MDD	6 weeks The trial had a 7 ± 4 days of PLB LI planned but was not followed strictly. The LO varied as well****	IMI	**42Y F patient, on day 11.** Suicidal ideation This event was only noted in the all adverse event listings and no further information is available as there was no patient narrative.
0600B 1-384-US/EU/ CA	Sept. 1997	Nov. 1999	MDD	6 weeks The trial had a 7 ± 4 days of PLB LI planned but was not followed strictly. The LO varied as well****	IMI	**56Y F patient , on day 14** Depression and suicidal ideation This event was only noted in the all adverse event listings and no further information is available as there was no patient narrative.
0600B 1-384-US/EU/ CA	Sept. 1997	Nov. 1999	MDD	6 weeks The trial had a 7 ± 4 days of PLB LI planned but was not followed strictly. The LO varied as well****	IMI	**31Y F patient, on day 2** Suicidal ideation This event was only noted in the all adverse event listings and no further information is available as there was no patient narrative.
0600B 1-384-	Sept. 1997	Nov. 1999	MDD	6 weeks	PLB	**58Y F patient, on day 13** Suicidal ideation

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on suicidal ideation
US/EU/ CA				The trial had a 7 ± 4 days of PLB LI planned but was not followed strictly. The LO varied as well****		This event was only noted in the all adverse event listings and no further information is available as there was no patient narrative.
0600B 1-384-US/EU/ CA	Sept. 1997	Nov. 1999	MDD	6 weeks The trial had a 7 ± 4 days of PLB LI planned but was not followed strictly. The LO varied as well****	PLB	**39Y M patient, on day 4** Black ideas (suicidal thoughts): Moderate "*On 7 Sep 98, the patient was hospitalized because of suicidal ideation."*
0600B 1-384-US/EU/ CA	Sept. 1997	Nov. 1999	MDD	6 weeks The trial had a 7 ± 4 days of PLB LI planned but was not followed strictly. The LO varied as well****	PLB	21Y F patient, on day 25 Increasing suicidal thoughts "*On 25 Mar 98, the study drug was discontinued because of severe anxiety and increasing suicidal thoughts. Because of the severe risk to the patient, the study code was broken. It was found that the patient had been assigned placebo. The patient was hospitalized and Effexor therapy was begun."*
0600A1-372-US	Sept. 1995	June 1997	MDD	6 weeks The trial had a 7 ± 3 days of PLB LI and up to 3 weeks of taper LO	PLB	**45Y M patient, on day 34** Increased suicidal ideation *"This 45-year-old man was randomly assigned to receive placebo on 12 December 1995. On 14 January 1996, study day 34, he reported increased suicidal ideation for the previous 2 days after receiving a very poor evaluation at work. The patient was hospitalized and study drug treatment was discontinued. He was hospitalized for 4 days and his suicidal ideation resolved. He began receiving antidepressant therapy...."*
0600B-209-US	Dec. 1994	Aug. 1995	MDD	8 weeks The trial had a 7 ± 3 days of PLB LI and up to 2 weeks of taper LO	PLB	**36Y F patient, on day 12 and day 39 (2 events)** Suicidal ideation (severe) *"This 36-year-old woman was randomly assigned to receive placebo on 2 March 1995. On 14 March 1995, study day 13, the patient developed suicidal ideation and study drug treatment was*

Trial	Start date FPFV	End date LPLV	Condition	Duration of acute phase	Drug and daily dose	Case notes on suicidal ideation
						discontinued. The patient was hospitalized on 15 March 1995. The patient received ECT therapy and was discharged from the hospital on 6 April 1995 on imipramine and Klonopin. The patient was readmitted to the hospital on 10 April 1995 because of suicidal ideation."

DLX: duloxetine; IMI: imipramine; PAR: paroxetine; SER: sertraline; VEN: venaflaxine; VEN ER venaflaxine extended release; PLB: placebo
Aug.: August; Feb.: February; Dec.; December; GSP: generalized social phobia; Jan.: January; MDD: major depressive disorder; Nov.; November; OCD: obsessive compulsive disorder; Oct.: October; PD: panic disorder; PTSD: posttraumatic stress disorder; SAD: social anxiety disorder; Sept.: September; SP: social phobia

Supplementary data Table 10 The number of suicidal ideation (SI) events in lead-out (LO) or post therapy (PT): 7 events in 7 patients, all on SSRIs (one on duloxetine, three on paroxetine, two on sertraline and one on venlaflaxine).

Trial	Start date FPFV	End date LPLV	Condition	Study duration	Drug and daily dose	Case notes on suicidal ideation
HMATb	March 2000	Feb. 2001	MDD	During LO The study had an 8 weeks acute phase and a 2 weeks PLB LO phase	DLX 20mg	**No patient details available, at v9 (exact day is unknown)** Passive suicidal ideation This event was only noted in the all adverse event listings and no further information is available as there was no patient narrative.
Protocol 329	April 1994	Feb. 1998	MDD paediatric	Post therapy Study had an 8 weeks acute phase and no PLB LI phase and no LO phase	PAR Dose unknown	**15Y F patient, about 111 days from start of study (exact number of days post treatment is unknown)** Threatened suicide "*....On 27-June-1995, the patient received her first dose of study medication. On 15-September-1995, the patient had to be hospitalized after an argument. She had become combative with her mother and had threatened suicide. She was prescribed Zoloft. Several days before her hospitalization, she had not taken her study medication. At the time of discharge, the patient was experiencing some depressive symptoms. In the opinion of the investigator, the event was probably not related to the study medication but to the parent's primary condition and family problems...."*

Trial	Start date FPFV	End date LPLV	Condition	Study duration	Drug and daily dose	Case notes on suicidal ideation
Protocol 651	Feb. 1999	Jan. 2000	PTSD	Post therapy Study had 12 weeks of acute phase with 2 weeks of taper LO	PAR 20mg	**27Y F patient, 13 days after last dose** Suicidal ideation with a plan, auditory hallucinations *"...This report refers to a 27-year-old female....On 04-August-1999, the patient received the first dose of blinded study medication for Posttraumatic Stress Disorder (PTSD). On 24-0ctober-1999, the patient discontinued use of blinded study medication on the recommendation of her primary care physician who had prescribed Norflex (orphenadrine citrate), codeine, Flexaril (cyclobenzaprine hydrochloride, and Valium (diazepam) for back pain. This event is cited on the patient's case report form as an adverse experience leading to withdrawal from the study. She missed her visit 8 appointment scheduled for 27-0ctober-1999 and missed the rescheduled appointment on 29-0ctober-1999. On 02-November-1999, 90 days after receiving the first dose of medication, and 13 days after discontinuing study medication, the patient's husband called the site and reported that the patient was experiencing a "panic attack" after a family argument. He stated that the patient was "hearing voices again." The patient expressed suicidal ideation with a plan, and verbalized that the voices told her "to take all the pills in the house." The patient was admitted to a hospital later that evening...."*
Protocol 627	July 1998	Jan. 2000	PTSD	Up to 3 weeks of double blind tapering LO phase, followed by 14 days PT (but could range from 2 to 6 weeks PT) The trial had a 1 week PLB LI and an acute phase of 12 weeks.	PAR	**41Y F patient, 6 days after last dose.** Suicidal ideation *"....The patient had a history of depression and anxiety. The patient received oral study medication from 25 September 1999 until 14 December 1999. On 20 December 1999, some 6 days after the last dose, the patient experienced insomnia, loss of appetite, anergia and disinterest. Later, the patient also experienced amotivation, poor concentration, negative and pessimistic thoughts, hopelessness and thoughts of death. Relevant tests included a computed tomography scan which was normal. The patient was diagnosed as having worsening major depression and suicidal ideation. The patient was treated for the event with paroxetine, alprazolam and zopiclone. Each of these events lasted 37 days. The investigator considered this to be a serious event because it was life threatening, disabling,*

Trial	Start date FPFV	End date LPLV	Condition	Study duration	Drug and daily dose	Case notes on suicidal ideation
						incapacitating and resulted in hospitalisation." This event was noted as worsening depression and only clarified as a SI through the patient narrative.
95CE21-0671	May 1996	June 1997	PTSD	No LO phase The study had 2weeks PLB LI phase and 12 weeks of acute therapy	SER	**47Y F patient, 17 days after last dose** Suicidal ideation (mild) This event was only noted in the all adverse event listings and no further information is available as there was no patient narrative.
R - 96ce21-0682	July 1996	Jan. 1998	PTSD	No LO phase The study had a 2 week PLB LI phase and 12 weeks of acute phase	SER 20mg	**24Y F patient, about 11 days after last dose and on day 95 of study** Threatened suicide by stabbing with a knife *"...patient started randomised therapy on sertraline with 25 mg daily on 5/21/97. Dosage was titrated until reaching 200 mg daily beginning 6/16/97 and remained at that until completing the study on 8/12/97. On 8/23/97, the subject threatened to commit suicide and attempted to stab herself with a knife. The subject was admitted to the hospital as a precautionary measure, and was treated with sertraline beginning 8/24/97. The suicidal ideation resolved on 8/27/97...."*
0600B-367-EU	Oct. 1994	Sept. 1995	MDD	Post therapy The study had a 7 ± 10 days f PLB LI with 8 weeks of acute phase and up to 3 days of taper LO phase	VEN 75mg	**28Y M patient, 4 days after last dose** Suicidal feeling *"This 28-year-old male patient was screened for his suitability for the study on May 31, 1995 and was randomly assigned to receive venlafaxine ER 75 mg/day on June 7, 1995. ...on August 10, the patient reported that he was feeling suicidal. This was after having been fired from work and therefore these feelings were not considered study drug related by the investigator. The patient completed the study and took his last dose of active study medication on August 6."*

DLX: duloxetine; IMI: imipramine; PAR: paroxetine; SER: sertraline; VEN: venaflaxine; VEN ER venaflaxine extended release; PLB: placebo

Aug.: August; Feb.: February; Dec.; December; GSP: generalized social phobia; Jan.: January; MDD: major depressive disorder; Nov.; November; Oct.: October; PTSD: posttraumatic stress disorder; Sept.: September